Jan Delaval

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Title of Invention: _____

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Jan Delaval
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L43 ANSWER 1 OF 11 MEDLINE
AN 97092867 MEDLINE
DN 97092867 PubMed ID: 8938429
TI Long-range map of a 3.5-Mb region in Xp11.23-22 with a sequence-ready map from a 1.1-Mb gene-rich interval.
AU Schindelhauer D; Hellebrand H; Grimm L; Bader I; Meitinger T; Wehnert M; Ross M; Meindl A
CS Abteilung fur Padiatrische Genetik, Kinderpoliklinik der Universitat Munchen, Germany.
SO GENOME RESEARCH, **(1996 Nov)** 6 (11) 1056-69.
Journal code: 9518021. ISSN: 1088-9051.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-H21088; GENBANK-R37743; GENBANK-U66359; GENBANK-Z37986
EM 199702
ED Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970227
AB Most of the yeast artificial chromosomes (YACs) isolated from the Xp11.23-22 region have shown instability and chimerism and are not a reliable resource for determining physical distances. We therefore constructed a long-range pulsed-field gel electrophoresis map that encompasses approximately 3.5 Mb of genomic DNA between the loci TIMP and DXS146 including a CpG-rich region around the WASP and TFE-3 gene loci. A combined YAC-cosmid contig was constructed along the genomic map and was used for fine-mapping of 15 polymorphic microsatellites and 30 expressed sequence tags (ESTs) or sequence transcribed sites (STSs), revealing the following order: tel-(SYN-TIMP)-(DXS426-ELK1)-ZNF(CA) n-L1-DXS1367-ZNF81-ZNF21-DXS6616- (HB3-OATL1pseudogenes-DXS6950)-DXS6949-DXS694 1-DXS7464E(MG61)-GW1E(EBP)- DXS7927E(MG81)-RBM- DXS722-DXS7467E(MG21)-DXS1011E-WASP-DXS6940++ +-DXS7466E(MG44)-GF1- DXS226-DXS1126-DXS1240-HB1-DXS7469E-(DXS6665-DXS1470)-TFE3-DXS7468E-+ ++SYP-DXS1208-HB2E-DXS573-DXS1331- DXS6666-DXS1039-DXS 1426-DXS1416-DXS7647-DXS8222-DXS6850-DXS255++ +-CIC-5-DXS146-cen. A sequence-ready map was constructed for an 1100-kb gene-rich interval flanked by the markers HB3 and DXS1039, from which six novel ESTs/STSs were isolated, thus increasing the number of markers used in this interval to thirty. This precise ordering is a prerequisite for the construction of a transcription map of this region that contains numerous disease loci, including those for several forms of retinal degeneration and mental retardation. In addition, the map provides the base to delineate the corresponding syntenic region in the mouse, where the mutants **scurfy** and tattered are localized.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Base Sequence
***Chromosome Mapping**

Chromosomes, Artificial, Yeast
Cosmids: GE, genetics
DNA Probes: GE, genetics
Electrophoresis, Gel, Pulsed-Field
Genetic Markers: GE, genetics
Mice
Microsatellite Repeats
Molecular Sequence Data
Sequence Analysis
***X Chromosome: GE, genetics**
Zinc Fingers: GE, genetics
CN 0 (Chromosomes, Artificial, Yeast); 0 (Cosmids); 0 (DNA Probes); 0 (Genetic Markers)

L43 ANSWER 2 OF 11 MEDLINE
AN 96152740 MEDLINE
DN 96152740 PubMed ID: 8566060
TI Disease in the **scurfy** (**sf**) mouse is associated with overexpression of cytokine genes.
AU Kanangat S; Blair P; Reddy R; Deheshia M; Godfrey V; Rouse B T; Wilkinson E
CS Department of Microbiology, College of Veterinary Medicine, University of Tennessee, Knoxville 37996, USA.
NC A132153
SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1996 Jan)** 26 (1) 161-5.
Journal code: 1273201. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603
ED Entered STN: 19960315
Last Updated on STN: 19960315
Entered Medline: 19960306
AB The murine X-linked lymphoproliferative disease **scurfy** is similar to the Wiskott-Aldrich syndrome in humans. Disease in **scurfy** (**sf**) mice is mediated by CD4+ T cells. Based on similarities in **scurfy** mice and transgenic mice that overexpress specific cytokine genes, we evaluated the expression of cytokines in the lesions of **sf** mice by Northern blotting, quantitative reverse-transcription polymerase chain reaction (RT-PCR) and by hybridization in situ. Overall, the phenotypic characteristics of **scurfy** disease correlated well with increased interleukin (IL)-4 (lymphadenopathy), IL-6 (B cell proliferation, hypergammaglobulinemia), IL-7 (dermal inflammatory cell infiltration), and high levels of tumor necrosis factor-alpha (wasting).
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Base Sequence
Blotting, Northern
***Cytokines: BI, biosynthesis**
***Cytokines: GE, genetics**
Disease Models, Animal
Gene Expression Regulation: IM, immunology
Interleukin-4: BI, biosynthesis
Interleukin-4: GE, genetics
Interleukin-6: BI, biosynthesis
Interleukin-6: GE, genetics
Interleukin-7: BI, biosynthesis
Interleukin-7: GE, genetics
Mice
Mice, Mutant Strains
Molecular Sequence Data

Polymerase Chain Reaction
T-Lymphocytes: ME, metabolism
Transcription, Genetic: IM, immunology
*Wiskott-Aldrich Syndrome: GE, genetics
Wiskott-Aldrich Syndrome: IM, immunology
RN 207137-56-2 (Interleukin-4)
CN 0 (Cytokines); 0 (Interleukin-6); 0 (Interleukin-7)

L43 ANSWER 3 OF 11 MEDLINE
AN 96115600 MEDLINE
DN 96115600 PubMed ID: 8666397
TI The mouse homolog of the Wiskott-Aldrich syndrome protein (WASP) gene is highly conserved and maps near the **scurfy** (**sf**) mutation on the X chromosome.
AU Derry J M; Wiedemann P; Blair P; Wang Y; Kerns J A; Lemahieu V; Godfrey V L; Wilkinson J E; Francke U
CS Howard Hughes Medical Institute, Stanford University Medical Center, California 94305, USA.
SO GENOMICS, **(1995 Sep 20)** 29 (2) 471-7.
Journal code: 8800135. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960819
Last Updated on STN: 19960819
Entered Medline: 19960807
AB The mouse WASP gene, the homolog of the gene mutated in Wiskott-Aldrich syndrome, has been isolated and sequenced. the predicted amino acid sequence is 86% identical to the human WASP sequence. A distinct feature of the mouse gene is an expanded polymorphic GGA trinucleotide repeat that codes for polyglycine and varies from 15 to 17 triplets in different Mus musculus strains. The genomic structure of the mouse WASP gene is expressed as an approximately 2.4-kb mRNA in thymus and spleen. Chromosomal mapping in an interspecific M. Musculus/M. spretus backcross placed the Wasp locus near the centromere of the mouse X chromosome, inseparable from Gata1, Tcfe3, and **scurfy** (**sf**). This localization makes Wasp a candidate for involvement in **scurfy**, a T cell-mediated fatal lymphoreticular disease of mice that has previously been proposed as a mouse homolog of Wiskott-Aldrich syndrome. Northern analysis of **sf** tissue samples indicated the presence of WASP mRNA in liver and skin, presumably as a consequence of lymphocytic infiltration, but non abnormalities in the amount or size of mRNA present.
CT Check Tags: Animal; Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Amino Acid Sequence
Base Sequence
Chromosome Mapping
Crosses, Genetic
Genomic Library
Linkage (Genetics)
Mice
Mice, Inbred Strains: GE, genetics
Molecular Sequence Data
Polymerase Chain Reaction
Proteins: CH, chemistry
***Proteins: GE, genetics**
Sequence Homology, Amino Acid
Sequence Homology, Nucleic Acid
*Wiskott-Aldrich Syndrome: GE, genetics
***X Chromosome**
CN 0 (Proteins); 0 (WASP protein)

L43 ANSWER 4 OF 11 MEDLINE
AN 95152175 MEDLINE
DN 95152175 PubMed ID: 7849405
TI The mouse **scurfy** (**sf**) mutation is tightly linked to Gata1 and Tfe3 on the proximal X chromosome.
AU Blair P J; Carpenter D A; Godfrey V L; Russell L B; Wilkinson J E; Rinchik E M
CS University of Tennessee, Oak Ridge Graduate Program of Biomedical Science 37831-8077.
SO MAMMALIAN GENOME, **(1994 Oct)** 5 (10) 652-4.
Journal code: 9100916. ISSN: 0938-8990.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950316
CT Check Tags: Animal; Female; Human; Male
Chromosome Mapping
Crosses, Genetic
Disease Models, Animal
Genes, Recessive
***Linkage (Genetics)**
Lymphatic Diseases: GE, genetics
Mice
Mice, Mutant Strains
Muridae
***Mutation**
Wiskott-Aldrich Syndrome: GE, genetics
***X Chromosome**
GEN Gata1; Tfe3; **sf**

L43 ANSWER 5 OF 11 MEDLINE
AN 95015867 MEDLINE
DN 95015867 PubMed ID: 7930593
TI CD4+CD8- T cells are the effector cells in disease pathogenesis in the **scurfy** (**sf**) mouse.
AU Blair P J; Bultman S J; Haas J C; Rouse B T; Wilkinson J E; Godfrey V L
CS Biology Division, Oak Ridge National Laboratory, TN 37831-8077.
NC A132153
SO JOURNAL OF IMMUNOLOGY, **(1994 Oct 15)** 153 (8) 3764-74.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; AIDS
EM 199411
ED Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941110
AB Mice hemizygous for the X-linked mutation, **scurfy** (**sf**), exhibit a fatal lymphoreticular disease that is mediated by T lymphocytes. To evaluate the respective roles of CD4 or CD8 single positive T cells in **scurfy** disease, neonates were treated with mAbs directed against the CD4 or CD8 molecules. Whereas mice treated with an anti-CD8 Ab developed lesions and succumbed to disease at the same time (17 days) as their untreated **scurfy** littermates, mice treated with an anti-CD4 Ab lived up to 11 wk before developing **scurfy** disease. To insure a more complete elimination of the T cell subsets, the **scurfy** mutation was bred onto beta 2-microglobulin (beta

2m)-deficient (CD8-less) and CD4-deficient transgenic mouse lines. Whereas there was little moderation of disease in beta 2m-deficient **scurfy** mice, CD4-deficient **scurfy** mice had markedly decreased **scurfy** lesions and a prolonged life span, similar to that of anti-CD4-treated **sf**/Y mice. Additionally, **scurfy** disease was transplanted into H-2-compatible nude mice through the adoptive transfer of CD4+CD8- T cells, but not CD4-CD8+ T cells. Flow-cytometric analysis revealed that **sf**/Y mice have an increased percentage of activated CD4+ T cells in their lymph nodes. In addition, there is an increase in the in vitro production of cytokines in the cultured splenocytes of CD8-less, but not CD4-less, **scurfy** mice. These data suggest that CD4+ T cells are critical mediators of disease in the **scurfy** mouse.

CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
***CD4-Positive T-Lymphocytes: IM, immunology**
CD8-Positive T-Lymphocytes: IM, immunology
Cytokines: ME, metabolism
Immunity, Cellular
Immunologic Deficiency Syndromes: IM, immunology
Immunophenotyping
Lymphocyte Depletion
Lymphoproliferative Disorders: GE, genetics
*Lymphoproliferative Disorders: IM, immunology
Mice
*Mice, Mutant Strains: IM, immunology
Mice, Nude
***T-Lymphocyte Subsets: IM, immunology**
beta 2-Microglobulin: DF, deficiency
CN 0 (Cytokines); 0 (beta 2-Microglobulin)

L43 ANSWER 6 OF 11 MEDLINE
AN 94330500 MEDLINE
DN 94330500 PubMed ID: 8053488
TI Transplantation of T cell-mediated, lymphoreticular disease from the **scurfy** (**sf**) mouse.
AU Godfrey V L; Rouse B T; Wilkinson J E
CS Biology Division, Oak Ridge National Laboratory, TN 37831-8077.
SO AMERICAN JOURNAL OF PATHOLOGY, **(1994 Aug)** 145 (2) 281-6.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199409
ED Entered STN: 19940914
Last Updated on STN: 19940914
Entered Medline: 19940908
AB The X-linked mutation, **scurfy** (**sf**), causes a fatal lymphoreticular disease characterized by runting, lymphadenopathy, splenomegaly, hypergammaglobulinemia, exfoliative dermatitis, Coombs'-positive anemia, and death by 24 days of age. T lymphocytes are required to mediate this syndrome as shown by a total absence of disease in mice bred to be **scurfy** and nude (**sf**/Y; nu/nu). The **scurfy** phenotype is not transmitted by **sf**/Y bone marrow transplants, though cells of **scurfy** origin do reconstitute all lymphoid organs in the recipient mouse. These data suggest that **scurfy** disease results from an abnormal T cell development process and not from an intrinsic stem cell defect. We therefore tested the ability of transplanted **scurfy** thymuses to transmit **scurfy** disease to congenic euthymic mice, to athymic (nude) mice, and to severe combined immunodeficiency (SCID) mice. Euthymic recipients of **sf**/Y thymic grafts remained clinically normal as did all SCID

and nude recipients of normal thymus transplants. Morphological lesions similar to those found in **scurfy** mice occurred in all H-2-compatible nude and SCID recipients of **sf**/Y thymic grafts. Intraperitoneal injections of **scurfy** thymocytes, splenocytes, and lymph node cells also transmitted the **scurfy** phenotype to H-2-compatible nude mice and SCID mice. Our findings indicate that **scurfy** disease can be transmitted to T cell-deficient mice by engraftment of **scurfy** T cells, but that pathogenic **scurfy** T cell activities can be inhibited (or prevented) in immunocompetent recipient mice.

CT Check Tags: Animal; Female; Male; Support, U.S. Gov't, Non-P.H.S.
Colon: PA, pathology
*Lymphoid Tissue: TR, transplantation
*Lymphoproliferative Disorders: ET, etiology
*Lymphoproliferative Disorders: GE, genetics
Lymphoproliferative Disorders: PA, pathology
Mice
*Mice, Mutant Strains: GE, genetics
***T-Lymphocytes: PH, physiology**
*Thymus Gland: TR, transplantation

L43 ANSWER 7 OF 11 MEDLINE
AN 93160626 MEDLINE
DN 93160626 PubMed ID: 8431636
TI Partial inversion of gene order within a homologous segment on the X chromosome.
AU Laval S H; Boyd Y
CS Genetics Division, Medical Research Council Radiobiology Unit, Didcot, Oxon, UK.
SO MAMMALIAN GENOME, **(1993)** 4 (2) 119-23.
Journal code: 9100916. ISSN: 0938-8990.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303
ED Entered STN: 19930402
Last Updated on STN: 19930402
Entered Medline: 19930316
AB The locus for the erthyroid transcription factor, GATA1, has been positioned in the small interval between DXS255 and TIMP on the proximal short arm of the human X Chromosome (Chr) by use of a partial human cDNA clone and a well-characterized somatic cell hybrid panel. Analysis of selected recombinants from 108 Mus musculus x Mus spretus backcross progeny with the same clone confirmed that the homologous murine locus (Gf-1) lies between Otc and the centromere of the mouse X Chr. These data imply that a partial inversion of gene order has occurred within the conserved segment that represents Xp21.1-Xp11.23 in human (CYBB-GATA1) and the proximal 6 cM of the mouse X Chr (Gf-1-Timp). Furthermore, they indicate that the mouse mutant **scurfy** and the human genetic disorder Wiskott-Aldrich syndrome, which have been mapped to the same regions as GATA1/Gf-1 in both species, may indeed be homologous disorders.
CT Check Tags: Animal; Female; Human; Male
Chromosome Mapping
Crosses, Genetic
***DNA-Binding Proteins: GE, genetics**
Hybrid Cells
***Inversion (Genetics)**
Mice
***Transcription Factors: GE, genetics**
***X Chromosome**
Zinc Fingers
RN 125267-48-3 (erythroid-specific DNA-binding factor)

CN 0 (DNA-Binding Proteins); 0 (Transcription Factors)
GEN Cybb; GATA1; Gf-1; Hprt; Maoa; Otc; Pfc; Timp

L43 ANSWER 8 OF 11 MEDLINE
AN 93120200 MEDLINE
DN 93120200 PubMed ID: 1477119
TI Two-dimensional polyacrylamide gel electrophoretic characterization of proteins from organs of C3H mice expressing the **scurfy** (**sf**) genetic mutation during early and late stages of disease progression.
AU Selkirk J K; Hite M C; Godfrey V; Merrick B A; He C; Griesemer R A; Daluge D R; Mansfield B K
CS Division of Toxicology Research and Testing, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina 27709.
SO APPLIED AND THEORETICAL ELECTROPHORESIS, **(1992)** 3 (2) 97-107. Journal code: 8915308. ISSN: 0954-6642.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
ED Entered STN: 19930226
Last Updated on STN: 19930226
Entered Medline: 19930205
AB **Scurfy** (**sf**), is an X-linked recessive lethal mutation that occurs spontaneously in the C3H mouse. The disease is characterized by lymphoid and hematopoietic dysfunction. Affected males are of small stature and exhibit scaliness and crusting of the eyelids, ears, tail, and feet, marked splenomegaly, moderate hepatomegaly, enlarged lymph nodes, and atrophy of the thymus. The average lifespan of the affected hemizygous males (**sf**/y) is 24 +/- 0.7 days. Total cellular proteins were extracted from pooled samples of thymus and spleen obtained from combined litters of mice. Tissue-specific protein profiles characteristic of either **sf** mutant or normal mice were analyzed by two dimensional polyacrylamide gel electrophoresis (2DPAGE) at different stages of the phenotypic expression of the **sf** mutation, to identify changes in protein patterns that might be associated with the progression of the disease. The resultant gels were silver stained, digitized, and analyzed, by image analysis utilizing a pipelined image processor connected to a host computer. At 14 +/- 1 days of age, protein patterns from **sf** mutant and normal mice control organs showed considerable homogeneity, although there were proteins identified unique to the **sf** mutant and to the normal controls. At 20 +/- 1 days of age, the pattern differences between the **sf** mutant and normal control increased markedly. Differences were expressed as the percent of proteins that were unique to either the **sf** mutant or the normal control from the total number of each type. The percent of proteins that increased or decreased in the three organs utilized in this study ranged between 21%-39% at 14 days and were between 25%-54% at 20 days. Differences in protein expression between the normal and **sf** mutant as the disorder progressed for each of the three tissues examined. In addition, thymus protein profiles from 9 day old littermates that were phenotypically normal but genotypically unknown were evaluated to determine if marker proteins could be identified for the **sf** mutation. Limited protein changes were noted at relative molecular weights of 66, 60, 54, 39, 37, 33, 25, 23, 27, and 11 kDa. These data suggest that the **sf** mutation follows a trackable pattern of protein expression and repression different than the normal control C3H mouse. Several potential marker proteins associated with the **sf** mutation were identified in 9 day thymus prior to the phenotypic expression of the disease. These putative biomarkers may be useful for characterizing the **sf** mutation and the mutant may act a possible

model the Wiskott-Aldrich syndrome (WAS).
CT Check Tags: Animal; Female; Male
*Abnormalities, Multiple: GE, genetics
Abnormalities, Multiple: ME, metabolism
Abnormalities, Multiple: PA, pathology
Age Factors
Biological Markers
Densitometry
Disease Models, Animal
***Electrophoresis, Gel, Two-Dimensional**
Genes, Lethal
Genes, Recessive
Heterozygote
Image Processing, Computer-Assisted
Isoelectric Focusing
*Lymphoproliferative Disorders: GE, genetics
Lymphoproliferative Disorders: ME, metabolism
Lymphoproliferative Disorders: PA, pathology
Mice
Mice, Inbred C3H: GE, genetics
*Mice, Mutant Strains: GE, genetics
***Proteins: AN, analysis**
Silver Staining
Thymus Gland: CH, chemistry
Thymus Gland: PA, pathology
*Viscera: CH, chemistry
Wiskott-Aldrich Syndrome
X Chromosome
CN 0 (Biological Markers); 0 (Proteins)
GEN **sf**

L43 ANSWER 9 OF 11 MEDLINE
AN 91288497 MEDLINE
DN 91288497 PubMed ID: 2062835
TI Fatal lymphoreticular disease in the **scurfy** (**sf**) mouse requires T cells that mature in a **sf** thymic environment: potential model for thymic education.
AU Godfrey V L; Wilkinson J E; Rinchik E M; Russell L B
CS Biology Division, Oak Ridge National Laboratory, TN 37831-8077.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1991 Jul 1)** 88 (13) 5528-32.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199108
ED Entered STN: 19910825
Last Updated on STN: 19910825
Entered Medline: 19910802
AB Characteristic lesions in mice hemi- or homozygous for the X-linked mutation **scurfy** (**sf**) include lymphohistiocytic proliferation in the skin and lymphoid organs, Coombs' test-positive anemia, hypergammaglobulinemia, and death by 24 days of age. The role of the thymus in the development of fatal lymphoreticular disease in the **scurfy** mouse was investigated. Neonatal thymectomy doubles the life span of **scurfy** mice, moderates the histologic lesions, and prevents anemia, despite the continued presence of high levels of serum IgG. Animals bred to be nude and **scurfy** (nu/nu; **sf**/Y) are viable, fertile, and free of **scurfy** lesions. Bone marrow from **scurfy** mice can reconstitute lethally irradiated, H-2-compatible animals but does not transmit **scurfy** disease. We conclude, from these data, that **scurfy** lesions are mediated by T

lymphocytes that mature in an abnormal (**sf**) thymic environment.
CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.
Animals, Newborn: IM, immunology
Bone Marrow Transplantation
Genes, Lethal
Genes, Recessive
*Lymphoproliferative Disorders: PA, pathology
Mice
Mice, Mutant Strains
Mice, Nude
Phenotype
Skin: PA, pathology
Thymectomy
*Thymus Gland: PP, physiopathology
X Chromosome
GEN **sf**

L43 ANSWER 10 OF 11 MEDLINE
AN 91273113 MEDLINE
DN 91273113 PubMed ID: 2053595
TI X-linked lymphoreticular disease in the **scurfy** (**sf**) mutant mouse.
AU Godfrey V L; Wilkinson J E; Russell L B
CS Biology Division, Oak Ridge National Laboratory, TN 37831-8077.
SO AMERICAN JOURNAL OF PATHOLOGY, **(1991 Jun)** 138 (6) 1379-87.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199107
ED Entered STN: 19910811
Last Updated on STN: 19910811
Entered Medline: 19910725
AB **Scurfy** (**sf**) is a spontaneous, sex-linked, recessive mutation that maps to the extreme proximal portion of the X chromosome, about 2 centimorgans from sparse fur (spf). Hemizygotes for **sf** manifest several clinical disorders, evident at 14 days of age, including scaliness and crusting of the eyelids, ears, and tail, runting, reddening and swelling of the genital papilla, anemia, cachexia, and early death (average, 24 days). Our studies indicate that the phenotype of hemizygous **scurfy** is not, as has been suggested, a model for human X-linked ichthyosis, but appears to be a disease primarily affecting the lymphoreticular, and possibly the hematopoietic, systems. Gross lesions include marked splenomegaly, hepatomegaly, enlarged lymph nodes, and variable thickening of the ears. The characteristic histologic lesion is a lymphohistiocytic proliferation and infiltration of peripheral lymph nodes, spleen, liver, and skin. In routine hematoxylin and eosin-stained sections, these lesions efface lymph node architecture, thicken the dermis, and form nodular portal infiltrates in the liver. **Scurfy** lesions characteristically contain a population of large blastlike cells with round to oval nuclei, a vesicular chromatin pattern, and prominent single nucleoli. Mixed perivascular infiltrates of lymphocytes, macrophages, and granulocytes sometimes are found in kidney, heart, pancreas, lung, and mesenteries. There is excessive hematopoiesis in the liver and spleen. Cells expressing B220 or Thy-1 antigens localize to appropriate areas in the lymph nodes and spleen, but are rare in the portal infiltrates and are absent from the skin. There is a marked, polyclonal increase in serum IgG, severe Coombs'-positive anemia, and leukocytosis with atypical mononuclear cells. **Scurfy** mice are negative for antinuclear antibodies. Despite their morphologically aberrant lymphoreticular system, **scurfy** mice can exist in a conventional environment without evidence of opportunistic infection.

Raising **scurfy** mice in a specific-pathogen-free environment does not alter disease expression. Thus, while our findings indicate that **scurfy** disease may be the result of immune dysfunction, it is not a classic immunodeficiency.

CT Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.
Blood Cell Count
Germ-Free Life
Immunohistochemistry
Immunologic Diseases: BL, blood
*Immunologic Diseases: GE, genetics
Immunologic Diseases: PA, pathology
***Linkage (Genetics)**
Longevity
Lymph Nodes: ME, metabolism
Lymph Nodes: PA, pathology
Lymphatic Diseases: BL, blood
*Lymphatic Diseases: GE, genetics
Lymphatic Diseases: PA, pathology
Mice
*Mice, Mutant Strains: GE, genetics
Mice, Mutant Strains: IM, immunology
Mice, Mutant Strains: ME, metabolism
Recombination, Genetic
***X Chromosome**

L43 ANSWER 11 OF 11 MEDLINE
AN 90207210 MEDLINE
DN 90207210 PubMed ID: 2320565
TI The **scurfy** mouse mutant has previously unrecognized hematological abnormalities and resembles Wiskott-Aldrich syndrome.
AU Lyon M F; Peters J; Glenister P H; Ball S; Wright E
CS Medical Research Council Radiobiology Unit, Didcot, Oxon, United Kingdom.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1990 Apr)** 87 (7) 2433-7.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
ED Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900504
AB The X chromosome-linked **scurfy** (**sf**) mutant of the mouse is recognized by the scaliness of the skin from which the name is derived and results in death of affected males at about 3-4 weeks of age. Consideration of known man-mouse homologies of the X chromosome prompted hematological studies, which have shown that the blood is highly abnormal. The platelet and erythrocyte counts are both reduced and become progressively lower relative to normal as the disease progresses. There is gastrointestinal bleeding, and most animals appear to die of severe anemia. By contrast, the leukocyte count is consistently raised. Some animals showed signs of infection but it is not yet clear whether there is immunodeficiency. Other features include the scaly skin and apparently reduced lateral growth of the skin, conjunctivitis, and diarrhea in some animals. The mutant resembles Wiskott-Aldrich syndrome in man, which is characterized by thrombocytopenia, eczema, diarrhea, and immunodeficiency. The loci of the human and mouse genes lie in homologous segments of the X chromosome, although apparently in somewhat different positions relative to other gene loci. **Scurfy** differs from Wiskott-Aldrich syndrome in that **scurfy** males are consistently hypogonadal.
CT Check Tags: Animal; Female; Human; Male
Aging

Body Weight
Bone Marrow: PA, pathology
Chromosome Mapping
Crosses, Genetic
Erythrocyte Count
Leukocyte Count
Liver: PA, pathology
Megakaryocytes: PA, pathology
Mice
Mice, Inbred C3H
Mice, Mutant Strains
Platelet Count
Reference Values
Wiskott-Aldrich Syndrome: BL, blood
*Wiskott-Aldrich Syndrome: GE, genetics
Wiskott-Aldrich Syndrome: PA, pathology
***X Chromosome**

=> d l44 all tot

L44 ANSWER 1 OF 16 MEDLINE
AN **2002408677** IN-PROCESS
DN **22151424** PubMed ID: **12161590**
TI Clinical and molecular features of the immunodysregulation, polyendocrinopathy, enteropathy, X linked (IPEX) syndrome.
AU Wildin R S; Smyk-Pearson S; Filipovich A H
CS Department of Molecular and Medical Genetics, Oregon Health Sciences University, Mailcode MP350, 3181 SW Sam Jackson Park Road, Portland, OR 97201-3098, USA.. wild@alum.mit.edu
NC R21-DK60207 (NIDDK)
R29 DK47278 (NIDDK)
SO JOURNAL OF MEDICAL GENETICS, (2002 Aug) 39 (8) 537-45.
Journal code: 2985087R. ISSN: 1468-6244.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
OS OMIM-304790
ED Entered STN: 20020807
Last Updated on STN: 20020807
AB Immunodysregulation, polyendocrinopathy, enteropathy, X linked (IPEX, OMIM 304790) is a rare, recessive disorder resulting in aggressive autoimmunity and early death. Mutations in **FOXP3** have been identified in 13 of 14 patients tested. Research in the mouse model, **scurfy**, suggests that autoimmunity may stem from a lack of working regulatory T cells. We review published reports regarding the genetics, clinical features, immunology, pathology, and treatment of IPEX. We also report three new patients who were treated with long term immunosuppression, followed by bone marrow transplantation in two. IPEX can be differentiated from other genetic immune disorders by its genetics, clinical presentation, characteristic pattern of pathology, and, except for high IgE, absence of substantial laboratory evidence of immunodeficiency. While chronic treatment with immunosuppressive drugs may provide temporary benefit for some patients, it does not cause complete remission. Remission has been observed with bone marrow transplantation despite incomplete engraftment, but the long term outcome is uncertain.

L44 ANSWER 2 OF 16 MEDLINE
AN 2002168091 MEDLINE
DN 21897094 PubMed ID: 11900414
TI A transgenic mouse strain with antigen-specific T cells (RAG1KO/**sf**/OVA) demonstrates that the **scurfy** (**sf**) mutation

causes a defect in T-cell tolerization.
AU Zahorsky-Reeves Joanne L; Wilkinson J Erby
CS Department of Pathology, University of Tennessee College of Veterinary Medicine, Knoxville 37909, USA.
SO COMPARATIVE MEDICINE, (2002 Feb) 52 (1) 58-62.
Journal code: 100900466.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020320
Last Updated on STN: 20020405
Entered Medline: 20020404
AB The **scurfy** (**sf**) murine mutation causes severe lymphoproliferation, which results in death of hemizygous males (**sf**/Y) by 22 to 26 days of age. The CD4+ T cells are crucial mediators of this disease. Recent publications have not only identified this mutation as the genetic equivalent of the human disease X-linked neonatal diabetes mellitus, enteropathy, and endocrinopathy syndrome, but also have indicated that the defective protein-**scurfin**-is a new forkhead/winged-helix protein with a frameshift mutation, resulting in a product without the functional forkhead. These results have lead to speculation that the **scurfy** gene acts by disrupting the T-cell tolerance mechanism, resulting in hyperresponsiveness and lack of down-regulation. The Rag1KO/**sf**/Y OVA strain, with virtually 100% of its CD4+ T cells reactive strictly to ovalbumin (OVA) peptide 323-339, is an excellent model for determination of the **sf** mutation's ability to disrupt tolerance. We hypothesized that Rag1KO/**sf**/OVA mice would not be tolerant to antigen at a dose that tolerizes control animals. We found that splenic cells from Rag1KO/**sf**/Y OVA mice injected with the same dose of OVA peptide that induces tolerance in cells from control mice proliferate in vitro in response to OVA peptide. These results are consistent with a defect in the pathway responsible for peripheral T-cell tolerization.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
Antigens, Differentiation: IM, immunology
***CD4-Positive T-Lymphocytes: IM, immunology**
Dose-Response Relationship, Immunologic
Flow Cytometry
***Genes, RAG-1**
***Homeodomain Proteins: GE, genetics**
Homeodomain Proteins: IM, immunology
*Immune Tolerance: GE, genetics
*Immune Tolerance: IM, immunology
*Lymphoproliferative Disorders: GE, genetics
Lymphoproliferative Disorders: IM, immunology
Mice
Mice, Inbred Strains
Mice, Knockout
Mice, Transgenic
Mutation
Ovalbumin: IM, immunology
Spleen: CY, cytology
Spleen: IM, immunology
RN 128559-51-3 (RAG-1 protein); 9006-59-1 (Ovalbumin)
CN 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (Homeodomain Proteins)

L44 ANSWER 3 OF 16 MEDLINE
AN 2002042302 MEDLINE
DN 21618849 PubMed ID: 11768393
TI Novel mutations of **FOXP3** in two Japanese patients with immune dysregulation, polyendocrinopathy, enteropathy, X linked syndrome (IPEX).

AU Kobayashi I; Shiari R; Yamada M; Kawamura N; Okano M; Yara A; Iguchi A; Ishikawa N; Ariga T; Sakiyama Y; Ochs H D; Kobayashi K
SO JOURNAL OF MEDICAL GENETICS, (2001 Dec) 38 (12) 874-6.
Journal code: 2985087R. ISSN: 1468-6244.
CY England: United Kingdom
DT Letter
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020124
Last Updated on STN: 20020308
Entered Medline: 20020307
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Base Sequence
Child
Child, Preschool
DNA Mutational Analysis
***DNA-Binding Proteins: GE, genetics**
*Diabetes Mellitus, Insulin-Dependent: GE, genetics
Infant
Infant, Newborn
*Infant, Newborn, Diseases: GE, genetics
Japan
*Kidney Diseases: GE, genetics
Linkage (Genetics): GE, genetics
Mongoloid Race: GE, genetics
***Mutation: GE, genetics**
*Polyendocrinopathies, Autoimmune: GE, genetics
Syndrome
*Thyroiditis, Autoimmune: GE, genetics
X Chromosome: GE, genetics
CN 0 (DNA-Binding Proteins); 0 (**scurfin**)

L44 ANSWER 4 OF 16 MEDLINE
AN 2002002587 MEDLINE
DN 21622531 PubMed ID: 11753102
TI IPEX is a unique X-linked syndrome characterized by immune dysfunction, polyendocrinopathy, enteropathy, and a variety of autoimmune phenomena.
AU Bennett C L; Ochs H D
CS Division of Genetics and Development, University of Washington, Seattle, Washington 98195, USA.. cbenet@uwashington.edu
SO CURRENT OPINION IN PEDIATRICS, (2001 Dec) 13 (6) 533-8. Ref: 33
Journal code: 9000850. ISSN: 1040-8703.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020102
Last Updated on STN: 20020207
Entered Medline: 20020206
AB The rare syndrome known as IPEX (OMIM: 304930) is characterized by immune-dysfunction, polyendocrinopathy, enteropathy, and X-linked inheritance. The gene responsible for IPEX maps to Xp11.23-q13.3, a region of the X chromosome that also harbors the Wiskott-Aldrich syndrome gene (WASP). IPEX syndrome results from mutations of a unique DNA binding protein gene, **FOXP3**. Mutations invariably impair the seemingly essential forkhead domain of the protein, which is uniquely located in the carboxyl terminus, affecting protein function. In this review, we describe the identification of IPEX as a unique X-linked syndrome, the clinical features of IPEX, mutations of the immune-specific **FOXP3** DNA

binding protein, and bone marrow transplantation as a potential cure for the syndrome, which is usually lethal within the first year of life in affected males.

CT Check Tags: Animal; Human
Bone Marrow Transplantation
***DNA-Binding Proteins: GE, genetics**
Linkage (Genetics)
Mice
Mutation
*Polyendocrinopathies, Autoimmune: GE, genetics
Polyendocrinopathies, Autoimmune: TH, therapy
*Protein-Losing Enteropathies: GE, genetics
Protein-Losing Enteropathies: TH, therapy
Sequence Alignment
Syndrome
***X Chromosome: GE, genetics**

CN 0 (DNA-Binding Proteins); 0 (**scurfin**)

L44 ANSWER 5 OF 16 MEDLINE
AN 2001669006 MEDLINE
DN 21571694 PubMed ID: 11714795
TI The amount of **scurfin** protein determines peripheral T cell number and responsiveness.
AU Khattri R; Kasprowicz D; Cox T; Mortrud M; Appleby M W; **Brunkow M E**; Ziegler S F; **Ramsdell F**
CS Celltech R&D, Inc., Bothell, WA 98021, USA.
SO JOURNAL OF IMMUNOLOGY, (2001 Dec 1) 167 (11) 6312-20.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200201
ED Entered STN: 20011121
Last Updated on STN: 20020124
Entered Medline: 20020102
AB In the absence of the recently identified putative transcription factor **scurfin**, mice develop a lymphoproliferative disorder resulting in death by 3 wk of age from a pathology that resembles TGF-beta or CTLA-4 knockout mice. In this report, we characterize mice that overexpress the **scurfin** protein and demonstrate that these animals have a dramatically depressed immune system. Mice transgenic for the **Foxp3** gene (which encodes the **scurfin** protein) have fewer T cells than their littermate controls, and those T cells that remain have poor proliferative and cytolytic responses and make little IL-2 after stimulation through the TCR. Although thymic development appears normal in these mice, peripheral lymphoid organs, particularly lymph nodes, are relatively acellular. In a separate transgenic line, forced expression of the gene specifically in the thymus can alter thymic development; however, this does not appear to affect peripheral T cells and is unable to prevent disease in mice lacking a functional **Foxp3** gene, indicating that the **scurfin** protein acts on peripheral T cells. The data indicate a critical role for the **Foxp3** gene product in the function of the immune system, with both the number and functionality of peripheral T cells under the aegis of the **scurfin** protein.

CT Check Tags: Animal
CD4-Positive T-Lymphocytes: IM, immunology
CD4-Positive T-Lymphocytes: ME, metabolism
CD4-Positive T-Lymphocytes: PA, pathology
CD8-Positive T-Lymphocytes: IM, immunology
CD8-Positive T-Lymphocytes: ME, metabolism
CD8-Positive T-Lymphocytes: PA, pathology

Cells, Cultured
***DNA-Binding Proteins: BI, biosynthesis**
***DNA-Binding Proteins: GE, genetics**
DNA-Binding Proteins: PH, physiology
Gene Expression Regulation: IM, immunology
Histocytochemistry
Immunophenotyping
Lymphocyte Count
Lymphocyte Culture Test, Mixed
***Lymphocyte Transformation: GE, genetics**
Lymphocyte Transformation: IM, immunology
Lymphopenia: GE, genetics
Lymphopenia: IM, immunology
Lymphopenia: PA, pathology
Mice
Mice, Inbred BALB C
Mice, Inbred C57BL
Mice, Mutant Strains
Mice, Transgenic
***T-Lymphocyte Subsets: IM, immunology**
T-Lymphocyte Subsets: ME, metabolism
***T-Lymphocyte Subsets: PA, pathology**
Thymus Gland: IM, immunology
Thymus Gland: ME, metabolism
Thymus Gland: PA, pathology
Transgenes: IM, immunology

CN 0 (DNA-Binding Proteins); 0 (**scurfin**)

L44 ANSWER 6 OF 16 MEDLINE
AN 2001608891 MEDLINE
DN 21541391 PubMed ID: 11685453
TI A rare polyadenylation signal mutation of the **FOXP3** gene (AAUAAA-->AAUGAA) leads to the IPEX syndrome.
AU Bennett C L; **Brunkow M E**; **Ramsdell F**; O'Briant K C; Zhu Q; Fuleihan R L; Shigeoka A O; Ochs H D; Chance P F
CS Division of Genetics and Development, Department of Pediatrics, University of Washington School of Medicine, Box 356320, Seattle, WA 98195, USA.
SO IMMUNOGENETICS, (2001 Aug) 53 (6) 435-9.
Journal code: 0420404. ISSN: 0093-7711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011102
Last Updated on STN: 20020123
Entered Medline: 20011204
AB The mouse **scurfy** gene, **Foxp3**, and its human orthologue, **FOXP3**, which maps to Xp11.23-Xq13.3, were recently identified by positional cloning. Point mutations and microdeletions of the **FOXP3** gene were found in the affected members of eight of nine families with IPEX (immune dysfunction, polyendocrinopathy, enteropathy, X-linked; OMIM 304930). We evaluated a pedigree with clinically typical IPEX in which mutations of the coding exons of **FOXP3** were not detected. Our reevaluation of this pedigree identified an A-->G transition within the first polyadenylation signal (AAUAAA-->AAUGAA) after the stop codon. The next polyadenylation signal is not encountered for a further 5.1 kb. This transition was not detected in over 212 normal individuals (approximately 318 X chromosomes), excluding the possibility of a rare polymorphism. We suggest that this mutation is causal of IPEX in this family by a mechanism of nonspecific degradation of the **FOXP3** gene message.
CT Check Tags: Female; Human; Male

Cells, Cultured
DNA Mutational Analysis
DNA-Binding Proteins: BI, biosynthesis
***DNA-Binding Proteins: GE, genetics**
Linkage (Genetics)
***Mutation**
Pedigree
***Poly A: ME, metabolism**
*Polyendocrinopathies, Autoimmune: GE, genetics
RNA, Messenger: AN, analysis
Reverse Transcriptase Polymerase Chain Reaction
T-Lymphocytes: ME, metabolism
X Chromosome
RN 24937-83-5 (Poly A)
CN 0 (DNA-Binding Proteins); 0 (RNA, Messenger); 0 (**scurfin**)

L44 ANSWER 7 OF 16 MEDLINE
AN 2001532405 MEDLINE
DN 21463104 PubMed ID: 11483607
TI **Scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation.
AU Schubert L A; **Jeffery E**; Zhang Y; **Ramsdell F**; Ziegler S F
CS Immunology Program, Virginia Mason Research Center, Seattle, Washington 98101, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Oct 5) 276 (40) 37672-9. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011002
Last Updated on STN: 20020122
Entered Medline: 20011204
AB We have recently identified and cloned **Foxp3**, the gene defective in mice with the **scurfy** mutation. The immune dysregulation documented in these mice and in humans with mutations in the orthologous gene indicates that the **foxp3** gene product, **scurfin**, is involved in the regulation of T cell activation and differentiation. The autoimmune state observed in these patients with the immune dysregulation polyendocrinopathy, enteropathy, X-linked syndrome, or X-linked autoimmunity-allergic dysregulation syndrome also points to a critical role for **scurfin** in the regulation of T cell homeostasis. **FOXP3** encodes a novel member of the forkhead family of transcription factors. Here we demonstrate that this structural domain is required for nuclear localization and DNA binding. **Scurfin**, transiently expressed in heterologous cells, represses transcription of a reporter containing a multimeric forkhead binding site. Upon overexpression in CD4 T cells, **scurfin** attenuates activation-induced cytokine production and proliferation. We have identified FKH binding sequences adjacent to critical NFAT regulatory sites in the promoters of several cytokine genes whose expression is sensitive to changes in SFN abundance. Our findings indicate that the ability of **scurfin** to bind DNA, and presumably repress transcription, plays a paramount role in determining the amplitude of the response of CD4 T cells to activation.
CT Check Tags: Animal; Human
***CD4-Positive T-Lymphocytes: DE, drug effects**
CD4-Positive T-Lymphocytes: PH, physiology
COS Cells
Cells, Cultured
Cytokines: BI, biosynthesis

Cytokines: ME, metabolism
DNA: DE, drug effects
DNA: ME, metabolism
DNA-Binding Proteins: GE, genetics
***DNA-Binding Proteins: PD, pharmacology**
DNA-Binding Proteins: PH, physiology
Gene Silencing: DE, drug effects
Gene Silencing: PH, physiology
***Lymphocyte Transformation: DE, drug effects**
Lymphocyte Transformation: PH, physiology
Mutation
Transcription Factors: PH, physiology
***Transcription, Genetic: DE, drug effects**
Transcription, Genetic: PH, physiology
Transfection
RN 9007-49-2 (DNA)
CN 0 (Cytokines); 0 (DNA-Binding Proteins); 0 (Transcription Factors); 0 (**scurfin**); 0 (transcription factor NF-AT)

L44 ANSWER 8 OF 16 MEDLINE
AN 2001328318 MEDLINE
DN 21265946 PubMed ID: 11396442
TI Treatment of the immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) by allogeneic bone marrow transplantation.
CM Comment in: N Engl J Med. 2001 Sep 27;345(13):999-1000
AU Baud O; Goulet O; Canioni D; Le Deist F; Radford I; Rieu D; Dupuis-Girod S; Cerf-Bensussan N; Cavazzana-Calvo M; Brousse N; Fischer A; Casanova J L
CS Service d'Immunologie et d'Hematologie Pediatriques, H pital Necker-Enfants Malades, Paris, France.
SO NEW ENGLAND JOURNAL OF MEDICINE, (2001 Jun 7) 344 (23) 1758-62. Journal code: 0255562. ISSN: 0028-4793.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614
CT Check Tags: Case Report; Female; Human; Male
Anemia, Hemolytic: GE, genetics
*Anemia, Hemolytic: TH, therapy
Autoimmune Diseases: GE, genetics
*Autoimmune Diseases: TH, therapy
*Bone Marrow Transplantation
DNA-Binding Proteins: GE, genetics
Diabetes Mellitus, Insulin-Dependent: GE, genetics
*Diabetes Mellitus, Insulin-Dependent: TH, therapy
Diarrhea: GE, genetics
*Diarrhea: TH, therapy
Fatal Outcome
Infant
***Linkage (Genetics)**
Pedigree
Point Mutation
Polyendocrinopathies, Autoimmune: GE, genetics
Polyendocrinopathies, Autoimmune: TH, therapy
Syndrome
Transplantation, Homologous
X Chromosome
CN 0 (DNA-Binding Proteins); 0 (**scurfin**)

L44 ANSWER 9 OF 16 MEDLINE

AN 2001164244 MEDLINE
DN 21150882 PubMed ID: 11265635
TI The murine mutation **scurfy** (**sf**) results in an antigen-dependent lymphoproliferative disease with altered T cell sensitivity.
AU Zahorsky-Reeves J L; Wilkinson J E
CS Transplantation Biology Research Laboratory, Department of Cardiothoracic Surgery, Childrens Hospital Los Angeles, Los Angeles, CA 90027, USA.. jzahorskyreeves@chla.usc.edu
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (2001 Jan) 31 (1) 196-204. Journal code: 1273201. ISSN: 0014-2980.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329
AB The **scurfy** (**sf**) murine mutation results in a rapidly fatal lymphoproliferative disease, causing death by 26 days. Mature CD4+ T cells which tested hyperresponsive to T cell receptor (TCR) stimulation are involved. When **sf** was bred onto a transgenic line (DO11.10) in which 75 - 95 % of the T cells express TCR for ovalbumin (OVA) 323 - 339, **sf** / Y OVA mice had prolonged lifespans and less severe clinical symptoms compared to controls. However, **sf** / Y OVA mice eventually developed disease and died with manifestations similar to those of the original **sf** strain. The Rag1 knockout (KO) mouse, which cannot produce mature T (or B) cells without the addition of functional transgenes, was chosen for further breeding. The combination of Rag1 KO, the OVA transgene, and **sf** produced mice with 100 % of their mature DO11.10 alpha beta T cells reactive strictly to OVA peptide. None of these Rag1 - / - **sf** / Y OVA mice developed the **scurfy** disease. They retained central deletion capability in vivo, but demonstrated an altered in vitro response to OVA peptide. These results indicate that mice without TCR for endogenous antigens do not develop **scurfy** symptoms, and are consistent with the hypothesis that the **sf** mutation requires antigen stimulation to manifest disease, perhaps via altered TCR sensitivity.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Antigens, Differentiation: PH, physiology
Flow Cytometry
Homeodomain Proteins: PH, physiology
Immunophenotyping
*Lymphoproliferative Disorders: ET, etiology
Lymphoproliferative Disorders: IM, immunology
Mice
Mice, Knockout
Mutation
***Ovalbumin: IM, immunology**
***T-Lymphocytes: IM, immunology**
RN 128559-51-3 (RAG-1 protein); 9006-59-1 (Ovalbumin)
CN 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (Homeodomain Proteins)

L44 ANSWER 10 OF 16 MEDLINE
AN 2001140771 MEDLINE
DN 21102364 PubMed ID: 11160129
TI Escape from tolerance in the human X-linked autoimmunity-allergic disregulation syndrome and the **Scurfy** mouse.
CM Comment on: J Clin Invest. 2000 Dec;106(12):R75-81
AU Patel D D
CS Departments of Medicine and Immunology, Duke University Medical Center, Box 2632, 223 MSRB, Durham, North Carolina 27710, USA..

patel003@mc.duke.edu
SO JOURNAL OF CLINICAL INVESTIGATION, (2001 Jan) 107 (2) 155-7.
Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Commentary
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20020121
Entered Medline: 20010308
CT Check Tags: Animal; Human; Male
*Autoimmune Diseases: GE, genetics
Autoimmune Diseases: PA, pathology
Autoimmune Diseases: TH, therapy
CD4-Positive T-Lymphocytes: IM, immunology
DNA-Binding Proteins: GE, genetics
Disease Models, Animal
Hypergammaglobulinemia: GE, genetics
*Hypersensitivity: GE, genetics
Hypersensitivity: PA, pathology
Hypersensitivity: TH, therapy
*Immune Tolerance
Immunosuppressive Agents: TU, therapeutic use
Infant
Mice
Mutation
Palliative Care
Syndrome
Thymus Gland: IM, immunology
Wasting Syndrome: GE, genetics
***X Chromosome**
CN 0 (DNA-Binding Proteins); 0 (Immunosuppressive Agents); 0 (**scurfin**)

L44 ANSWER 11 OF 16 MEDLINE
AN 2001099631 MEDLINE
DN 20578751 PubMed ID: 11138001
TI Disruption of a new forkhead/winged-helix protein, **scurfin**, results in the fatal lymphoproliferative disorder of the **scurfy** mouse.
AU **Brunkow M E; Jeffery E W; Hjerrild K A;**
Paeper B; Clark L B; Yasayko S A; Wilkinson J E; Galas D; Ziegler S F; **Ramsdell F**
CS Celltech Chiroscience, Inc., Bothell, Washington, USA..
marybrunkow@chiroscience.com
SO NATURE GENETICS, (2001 Jan) 27 (1) 68-73.
Journal code: 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-A49395; GENBANK-AF196779; GENBANK-AF235097; GENBANK-AF277991; GENBANK-AF277992; GENBANK-AF277993; GENBANK-AF277994; GENBANK-AF277995; GENBANK-AF277996; GENBANK-AF318279; GENBANK-AF318280; GENBANK-AF318281; GENBANK-AJ005891; GENBANK-U93305; GENBANK-X97571
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201
AB **Scurfy** (**sf**) is an X-linked recessive mouse mutant resulting in lethality in hemizygous males 16-25 days after birth, and is

characterized by overproliferation of CD4+CD8- T lymphocytes, extensive multiorgan infiltration and elevation of numerous cytokines. Similar to animals that lack expression of either Ctla-4 or Tgf-beta, the pathology observed in **sf** mice seems to result from an inability to properly regulate CD4+CD8- T-cell activity. Here we identify the gene defective in **sf** mice by combining high-resolution genetic and physical mapping with large-scale sequence analysis. The protein encoded by this gene (designated **Foxp3**) is a new member of the forkhead/winged-helix family of transcriptional regulators and is highly conserved in humans. In **sf** mice, a frameshift mutation results in a product lacking the forkhead domain. Genetic complementation demonstrates that the protein product of **Foxp3**, **scurfin** , is essential for normal immune homeostasis.

CT Check Tags: Animal; Female; Human; Male
Amino Acid Motifs
Amino Acid Sequence
Cloning, Molecular
Conserved Sequence
DNA Mutational Analysis
***DNA-Binding Proteins: CH, chemistry**
DNA-Binding Proteins: GE, genetics
***DNA-Binding Proteins: ME, metabolism**
Gene Expression Profiling
***Genes, Essential: GE, genetics**
Genes, Recessive: GE, genetics
Genetic Complementation Test
Lymph Nodes: IM, immunology
Lymph Nodes: PA, pathology
Lymphocyte Count
*Lymphoproliferative Disorders: GE, genetics
Lymphoproliferative Disorders: IM, immunology
Lymphoproliferative Disorders: PA, pathology
Mice
Mice, Mutant Strains
Mice, Transgenic
Molecular Sequence Data
***Mutation: GE, genetics**
Phenotype
Physical Chromosome Mapping
Protein Structure, Tertiary
RNA, Messenger: AN, analysis
RNA, Messenger: GE, genetics
Sequence Alignment

CN 0 (DNA-Binding Proteins); 0 (RNA, Messenger); 0 (**scurfin**)

L44 ANSWER 12 OF 16 MEDLINE
AN 2001099620 MEDLINE
DN 20578743 PubMed ID: 11137993
TI The immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) is caused by mutations of **FOXP3**.
AU Bennett C L; Christie J; **Ramsdell F; Brunkow M E;** Ferguson P J; Whitesell L; Kelly T E; Saulsbury F T; Chance P F; Ochs H D
CS Division of Genetics and Development, Department of Pediatrics, University of Washington, Seattle, USA.
NC HD17427 (NICHD)
SO NATURE GENETICS, (2001 Jan) 27 (1) 20-1.
Journal code: 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200102
ED Entered STN: 20010322

Last Updated on STN: 20010322
Entered Medline: 20010201

AB IPEX is a fatal disorder characterized by immune dysregulation, polyendocrinopathy, enteropathy and X-linked inheritance (MIM 304930). We present genetic evidence that different mutations of the human gene **FOXP3**, the ortholog of the gene mutated in **scurfy** mice (**Foxp3**), causes IPEX syndrome. Recent linkage analysis studies mapped the gene mutated in IPEX to an interval of 17-20-cM at Xp11. 23-Xq13.3.

CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
DNA-Binding Proteins: CH, chemistry
***DNA-Binding Proteins: GE, genetics**
DNA-Binding Proteins: ME, metabolism
***Linkage (Genetics): GE, genetics**
Mice
Molecular Sequence Data
***Mutation: GE, genetics**
Pedigree
Phenotype
*Polyendocrinopathies, Autoimmune: GE, genetics
*Protein-Losing Enteropathies: GE, genetics
Sequence Alignment
Syndrome
***X Chromosome: GE, genetics**

CN 0 (DNA-Binding Proteins); 0 (**scurfin**)

L44 ANSWER 13 OF 16 MEDLINE
AN 2001099619 MEDLINE
DN 20578742 PubMed ID: 11137992
TI X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is the human equivalent of mouse **scurfy**.
AU Wildin R S; **Ramsdell F**; Peake J; Faravelli F; Casanova J L; Buist N; Levy-Lahad E; Mazzella M; Goulet O; Perroni L; Bricarelli F D; Byrne G; McEuen M; Proll S; Appleby M; **Brunkow M E**
CS Department of Molecular and Medical Genetics, Oregon Health Sciences University, Portland, USA.. wildinr@ohsu.edu
SO NATURE GENETICS, (2001 Jan) 27 (1) 18-20.
Journal code: 9216904. ISSN: 1061-4036.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF235097; GENBANK-AF277993
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB To determine whether human X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome (IPEX; MIM 304930) is the genetic equivalent of the **scurfy** (**sf**) mouse, we sequenced the human ortholog (**FOXP3**) of the gene mutated in **scurfy** mice (**Foxp3**), in IPEX patients. We found four non-polymorphic mutations. Each mutation affects the forkhead/winged-helix domain of the **scurfin** protein, indicating that the mutations may disrupt critical DNA interactions.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
*Animal Diseases: GE, genetics
DNA Mutational Analysis
DNA-Binding Proteins: CH, chemistry
***DNA-Binding Proteins: GE, genetics**

DNA-Binding Proteins: ME, metabolism
*Diabetes Mellitus: CN, congenital
*Diabetes Mellitus: GE, genetics
Disease Models, Animal
Infant, Newborn
Linkage (Genetics): GE, genetics
Mice
Mice, Mutant Strains
Molecular Sequence Data
Mutation: GE, genetics
*Polyendocrinopathies, Autoimmune: GE, genetics
*Protein-Losing Enteropathies: GE, genetics
Sequence Alignment
Syndrome
***X Chromosome: GE, genetics**
CN 0 (DNA-Binding Proteins); 0 (**scurfin**)

L44 ANSWER 14 OF 16 MEDLINE
AN 2000412524 MEDLINE
DN 20313888 PubMed ID: 10857745
TI A transcript map of a 2-Mb BAC contig in the proximal portion of the mouse X chromosome and regional mapping of the **scurfy** mutation.
AU Means G D; Toy D Y; Baum P R; Derry J M
CS Immunex Corporation, Seattle, Washington 98101-2936, USA.
SO GENOMICS, (2000 May 1) 65 (3) 213-23.
Journal code: 8800135. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000828
AB A physical clone contig has been constructed, spanning 2 Mb on the proximal mouse X chromosome containing the mouse **scurfy** (**sf**) and tattered (Td) mutations. Extensive transcript mapping in this interval has identified 37 potential transcription units, including a number of novel genes, and 4 pseudogenes. These genes have been ordered by STS content and restriction mapping. Comparison of the transcript map to the corresponding region in human Xp11.23-p11.22 shows extensive homology, with complete conservation of gene order for loci in common between the two maps. Further, using a novel method to identify simple sequence length polymorphisms, we have developed a number of genetic markers, which has enabled the region containing the **sf** mutation to be narrowed to <300 kb. This contig has already allowed the cloning of the Td gene using a candidate gene approach and now serves as a starting point for the cloning of the **sf** mutation.
CT Check Tags: Animal; Female; Human; Male
Chromosomes, Bacterial
***Contig Mapping**
DNA, Complementary: GE, genetics
Haplotypes
*Lymphoproliferative Disorders: GE, genetics
Mice
Mice, Inbred C57BL
***Mutation**
***Transcription, Genetic**
***X Chromosome: GE, genetics**
CN 0 (DNA, Complementary)

L44 ANSWER 15 OF 16 MEDLINE
AN 2000222764 MEDLINE

DN 20222764 PubMed ID: 10754099
TI Molecular and genetic analysis of the mouse homolog of the Drosophila suppressor of position-effect variegation 3-9 gene.
AU Bultman S; Magnuson T
CS Department of Genetics, Case Western Reserve University, Cleveland, OH 22106, USA.
SO MAMMALIAN GENOME, (2000 Apr) 11 (4) 251-4.
Journal code: 9100916. ISSN: 0938-8990.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-L08238
EM 200005
ED Entered STN: 20000606
Last Updated on STN: 20000606
Entered Medline: 20000519
AB The Drosophila melanogaster gene suppressor of position-effect variegation 3-9 [Su(var)3-9] encodes a component of heterochromatin with a chromodomain and a SET domain. Here, we describe the cloning of a mouse homolog called Suv39h1 and describe the genomic organization, pattern of expression, and genetic map position. The genomic locus is approximately 10 kb and consists of five exons. The first two exons, 1a and 1b, are alternative first exons and are followed by three common exons. Two mRNAs, encompassing exon 1a or 1b, encode protein isoforms with distinct amino termini, but which are otherwise identical, including the chromodomain and SET domain. Interestingly, only one of the isoforms contains a putative nuclear localization signal. Consistent with other genes encoding proteins associated with chromatin structure, Suv39h1 is expressed in a widespread manner. Interspecific backcross mapping localized Suv39h1 near tattered (Td) and **scurfy** (**sf**) on the proximal X Chromosome (Chr). However, analysis of Td/Y and **sf**/Y mutant stocks indicated that Suv39h1 is not responsible for either mutant phenotype.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Base Sequence
Chromosome Mapping: VE, veterinary
DNA Primers
DNA, Complementary
*Drosophila melanogaster: GE, genetics
Exons
Introns
Mice
Molecular Sequence Data
***Repressor Proteins: GE, genetics**
CN 0 (DNA Primers); 0 (DNA, Complementary); 0 (Repressor Proteins); 0 (Su(var)3-9 protein)

L44 ANSWER 16 OF 16 MEDLINE
AN 1999172183 MEDLINE
DN 99172183 PubMed ID: 10072494
TI Cellular and molecular characterization of the **scurfy** mouse mutant.
AU Clark L B; Appleby M W; **Brunkow M E**; Wilkinson J E; Ziegler S F; **Ramsdell F**
CS Chiroscience R&D, Inc., Seattle, WA 98021, USA.
SO JOURNAL OF IMMUNOLOGY, (1999 Mar 1) 162 (5) 2546-54.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199904

ED Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990414

AB Mice hemizygous (Xsf/Y) for the X-linked mutation **scurfy** (**sf**) develop a severe and rapidly fatal lymphoproliferative disease mediated by CD4+CD8- T lymphocytes. We have undertaken phenotypic and functional studies to more accurately identify the immunologic pathway(s) affected by this important mutation. Flow cytometric analyses of lymphoid cell populations reveal that **scurfy** syndrome is characterized by changes in several phenotypic parameters, including an increase in Mac-1+ cells and a decrease in B220+ cells, changes that may result from the production of extremely high levels of the cytokine granulocyte-macrophage CSF by **scurfy** T cells. **Scurfy** T cells also exhibit strong up-regulation of cell surface Ags indicative of in vivo activation, including CD69, CD25, CD80, and CD86. Both **scurfy** and normal T cells are responsive to two distinct signals provided by the TCR and by ligation of CD28; **scurfy** cells, however, are hyperresponsive to TCR ligation and exhibit a decreased requirement for costimulation through CD28 relative to normal controls. This hypersensitivity may result, in part, from increased costimulation through B7-1 and B7-2, whose expression is up-regulated on **scurfy** T cells. Although the specific defect leading to this hyperactivation has not been identified, we also demonstrate that **scurfy** T cells are less sensitive than normal controls to inhibitors of tyrosine kinases such as genistein and herbimycin A, and the immunosuppressant cyclosporin A. One interpretation of our data would suggest that the **scurfy** mutation results in a defect, which interferes with the normal down-regulation of T cell activation.

CT Check Tags: Animal; Female; Male
Antigens, CD45: AN, analysis
Antigens, CD80: AN, analysis
Antigens, Differentiation: AN, analysis
Cyclosporine: PD, pharmacology
Genistein: PD, pharmacology
Granulocyte-Macrophage Colony-Stimulating Factor: BI, biosynthesis
Lymphocyte Transformation
*Lymphoproliferative Disorders: GE, genetics
Lymphoproliferative Disorders: IM, immunology
Mice
Mice, Inbred C3H
Mice, Mutant Strains
Nuclear Proteins: AN, analysis
Quinones: PD, pharmacology
Receptors, Antigen, T-Cell: PH, physiology
***T-Lymphocytes: IM, immunology**
Transcription Factors: AN, analysis

RN 446-72-0 (Genistein); 59865-13-3 (Cyclosporine); 70563-58-5 (herbimycin); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)

CN 0 (Antigens, CD45); 0 (Antigens, CD80); 0 (Antigens, Differentiation); 0 (CTLA-4); 0 (MAC1 protein); 0 (Nuclear Proteins); 0 (Quinones); 0 (Receptors, Antigen, T-Cell); 0 (Transcription Factors)

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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 August 2002 (20020814/ED)

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L61 ANSWER 1 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:435036 BIOSIS
DN PREV200200435036
TI Identification of the gene causing the mouse **scurfy** phenotype and its human ortholog.
AU **Brunkow, Mary E.; Jeffery, Eric W. (1); Hjerrild, Kathryn A.; Ramsdell, Fred**
CS (1) Seattle, WA USA
ASSIGNEE: Darwin Discovery Ltd., Cambridge, UK
PI US 6414129 July 02, 2002
SO Official Gazette of the United States Patent and Trademark Office Patents, (July 2, 2002) Vol. 1260, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB Isolated nucleic acid molecules are provided which encode **Fkhsf**, as well as mutant forms thereof. Also provided are expression vectors suitable for expressing such nucleic acid molecules, and host cells containing such expression vectors. Utilizing assays based upon the nucleic acid sequences disclosed herein (as well as mutant forms thereof), numerous molecules may be identified which modulate the immune system
NCL 536235000
CC Genetics and Cytogenetics - General *03502
IT Major Concepts
Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Chemicals & Biochemicals
gene
IT Methods & Equipment
gene identification: identification method
IT Miscellaneous Descriptors
scurfy phenotype

L61 ANSWER 2 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:270481 BIOSIS
DN PREV200200270481
TI A rare polyadenylation signal mutation of the **FOXP3** gene (AAUAAAfwdarwAAUGAA) leads to the **IPEX** syndrome.
AU Bennett, Craig L.; **Brunkow, Mary E.; Ramsdell, Fred;** O'Briant, Kathy C.; Zhu, Qili; Fuleihan, Ramsay L.; Shigeoka, Ann O.; Ochs, Hans D.; Chance, Phillip F. (1)
CS (1) Division of Genetics and Development, Department of Pediatrics, University of Washington School of Medicine, Seattle, WA, 98195: pchance@u.washington.edu USA
SO Immunogenetics, (August, 2001) Vol. 53, No. 6, pp. 435-439. print. ISSN: 0093-7711.
DT Article
LA English
AB The mouse **scurfy** gene, **Foxp3**, and its human orthologue, **FOXP3**, which maps to Xp11.23-Xq13.3, were recently identified by positional cloning. Point mutations and microdeletions of the **FOXP3** gene were found in the affected members of eight of nine families with **IPEX** (immune dysfunction, polyendocrinopathy, enteropathy, X-linked; OMIM 304930). We evaluated a pedigree with clinically typical **IPEX** in which mutations of the coding exons of **FOXP3** were not detected. Our reevaluation of this pedigree identified an AfwdarwG transition within the first polyadenylation signal (AAUAAAfwdarwAAUGAA) after the stop codon. The next polyadenylation signal

is not encountered for a further 5.1 kb. This transition was not detected in over 212 normal individuals (apprx318 X chromosomes), excluding the possibility of a rare polymorphism. We suggest that this mutation is causal of **IPEX** in this family by a mechanism of nonspecific degradation of the **FOXP3** gene message.

CC Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Human *03508
Immunology and Immunochemistry - General; Methods *34502
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Hominidae 86215
Muridae 86375

IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Medical Genetics (Allied Medical Sciences)

IT Parts, Structures, & Systems of Organisms
CD8 positive T cells: immune system; chromosome X: location p11.23, location q13.3

IT Diseases
X-linked immunodeficiency syndrome: genetic disease, immune system disease

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

GEN human **FOXP3** gene (Hominidae); mouse **foxp3** gene [mouse **scurfy** gene] (Muridae)

L61 ANSWER 3 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:514969 BIOSIS

DN PREV200100514969

TI **Scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation.

AU Schubert, Lisa A.; **Jeffery, Eric**; Zhang, Yi; **Ramsdell, Fred**; Ziegler, Steven F. (1)

CS (1) Dept. of Immunology, Virginia Mason Research Center, 1201 9th Ave., Seattle, WA, 98101: sziegler@vmresearch.org USA

SO Journal of Biological Chemistry, (October 5, 2001) Vol. 276, No. 40, pp. 37672-37679. print.
ISSN: 0021-9258.

DT Article

LA English

SL English

AB We have recently identified and cloned **Foxp3**, the gene defective in mice with the **scurfy** mutation. The immune dysregulation documented in these mice and in humans with mutations in the orthologous gene indicates that the **foxp3** gene product, **scurfin**, is involved in the regulation of T cell activation and differentiation. The autoimmune state observed in these patients with the immune dysregulation polyendocrinopathy, enteropathy, X-linked syndrome, or X-linked autoimmunity-allergic dysregulation syndrome also points to a critical role for **scurfin** in the regulation of T cell homeostasis. **FOXP3** encodes a novel member of the forkhead family of transcription factors. Here we demonstrate that this structural domain is required for nuclear localization and DNA binding. **Scurfin**, transiently expressed in heterologous cells, represses transcription of a reporter containing a multimeric forkhead binding site. Upon overexpression in CD4 T cells, **scurfin** attenuates activation-induced cytokine production and proliferation. We have

identified **FKH** binding sequences adjacent to critical NFAT regulatory sites in the promoters of several cytokine genes whose expression is sensitive to changes in SFN abundance. Our findings indicate that the ability of **scurfin** to bind DNA, and presumably repress transcription, plays a paramount role in determining the amplitude of the response of CD4 T cells to activation.

CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Immunology and Immunochemistry - General; Methods *34502

BC Muridae 86375

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, immune system

IT Chemicals & Biochemicals
DNA; **scurfin**

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae)

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

GEN mouse **Foxp3** gene (Muridae)

L61 ANSWER 4 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:258322 BIOSIS

DN PREV200100258322

TI Immune deficiency/dysregulation, Polyendocrinopathy, enteropathy, x-linked inheritance (**IPEX**) is caused by mutations of the human **scurfy** (**FOXP3**) gene.

AU Ochs, Hans D. (1); Bennett, Craig L. (1); Christie, Jacinda (1); **Ramsdell, Fred; Brunkow, Mary E.**; Ferguson, Polly J.; Whitesell, Luke; Sakiyama, Yukio; Barker, David F.; Shigeoka, Ann O.; Notarangelo, Luigi D.; Chance, Phillip F. (1)

CS (1) University of Washington, 1959 NE Pacific Street, Seattle, WA, 98195 USA

SO FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1014. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.

DT Conference

LA English

SL English

AB **IPEX** is a fatal congenital disorder characterized by Immune deficiency/dysregulation, Polyendocrinopathy and other autoimmune diseases. The responsible locus has been mapped to chromosome Xp11.23-Xq13.3. The murine disorder, **scurfy**, shares phenotypic features with **IPEX** and maps to a region of conserved synteny on the mous X-chromosome. The murine **scurfy** (**Foxp3**) gene was recently cloned, along with the human orthologue (**FOXP3**). The gene product was found to be a novel member of the forkhead family of DNA binding proteins. Murine **scurfy** is a congenital x-linked lethal disorder characterized by wasting, infections, scaly skin, diarrhea, anemia and thrombocytopenia. Leukocytosis and lymphadenopathy are characteristic and CD4+ T cells are hyper responsive to T cell stimulation and, if activated, secrete excessive cytokines. The **scurfy** mutation consists of a 2 base pair insertion upstream of the forkhead domain resulting in frameshift and premature termination. To

test the hypothesis that mutations of the **FOXP3** gene are the direct cause of **IPEX** we have examined **FOXP3** in 6 unrelated **IPEX** families. Six novel mutations were identified including missense mutations, nonsense mutations and deletions, mostly affecting the forkhead domain. In one family we found a 2 base pair deletion affecting the termination codon (Stop fwdarw Thr). These analyses strongly suggest that the **IPEX** phenotype observed in these families is due to mutations of **FOXP3**.

CC Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Human *03508
Endocrine System - General *17002
Developmental Biology - Embryology - Pathological *25503
Immunology and Immunochemistry - General; Methods *34502
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Hominidae 86215
Muridae 86375

IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis)

IT Parts, Structures, & Systems of Organisms
X chromosome

IT Diseases
IPEX: congenital disease, fatal; anemia: blood and lymphatic disease; autoimmune disease: immune system disease; enteropathy; leukocytosis: blood and lymphatic disease; lymphadenopathy: immune system disease; polyendocrinopathy: endocrine disease; thrombocytopenia: blood and lymphatic disease

IT Chemicals & Biochemicals
DNA binding proteins

IT Alternate Indexing
Anemia (MeSH); Autoimmune Diseases (MeSH); Leukocytosis (MeSH); Lymphatic Diseases (MeSH); Thrombocytopenia (MeSH)

IT Miscellaneous Descriptors
X-linked inheritance; Meeting Abstract

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
mouse (Muridae)

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

GEN human **FOXP3** gene (Hominidae): human **scurfy** gene

L61 ANSWER 5 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:81971 BIOSIS
DN PREV200100081971
TI Disruption of a new forkhead/winged-helix protein, **scurfin**, results in the fatal lymphoproliferative disorder of the **scurfy** mouse.
AU **Brunkow, Mary E. (1); Jeffery, Eric W.; Hjerrild, Kathryn A.**; Paeper, Bryan; Clark, Lisa B.; Yasayko, Sue-Ann; Wilkinson, J. Erby; Galas, David; Ziegler, Steven F.; **Ramsdell, Fred**
CS (1) Celltech Chiroscience, Inc., Bothell, WA: marybrunkow@chiroscience.com USA
SO Nature Genetics, (January, 2001) Vol. 27, No. 1, pp. 68-73. print.
ISSN: 1061-4036.

DT Article
LA English
SL English
AB **Scurfy** (**sf**) is an X-linked recessive mouse mutant resulting in lethality in hemizygous males 16-25 days after birth, and is characterized by overproliferation of CD4+CD8- T lymphocytes, extensive multiorgan infiltration and elevation of numerous cytokines. Similar to animals that lack expression of either Ctla-4 or Tgf-beta, the pathology observed in **sf** mice seems to result from an inability to properly regulate CD4+CD8- T-cell activity. Here we identify the gene defective in **sf** mice by combining high-resolution genetic and physical mapping with large-scale sequence analysis. The protein encoded by this gene (designated **Foxp3**) is a new member of the forkhead/winged-helix family of transcriptional regulators and is highly conserved in humans. In **sf** mice, a frameshift mutation results in a product lacking the forkhead domain. Genetic complementation demonstrates that the protein product of **Foxp3**, **scurfin** , is essential for normal immune homeostasis.
CC Immunology and Immunochemistry - General; Methods *34502
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
BC Muridae 86375
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Blood and Lymphatics (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
CD4-positive CD8-negative T lymphocytes: blood and lymphatics, immune system
IT Diseases
lymphoproliferative disorder: blood and lymphatic disease, genetic disease
IT Chemicals & Biochemicals
Ctla-4; **scurfin**: forkhead/winged-helix protein; transforming growth factor-beta
IT Alternate Indexing
Lymphoproliferative Disorders (MeSH)
IT Methods & Equipment
high-resolution genetic mapping: analytical method; high-resolution physical mapping: analytical method; large-scale sequence analysis: analytical method
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae): **scurfy** mutant
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L61 ANSWER 6 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:39857 BIOSIS
DN PREV200100039857
TI Cloning of the **scurfy** gene product indicates a role for a novel forkhead family protein in the regulation of T cell activation.
AU Schubert, L. A. (1); Ziegler, S. F.; **Brunkow, M.**; **Ramsdell, F.**

CS (1) Virginia Mason Research Center, Seattle, WA, 98101 USA
SO FASEB Journal, (April 20, 2000) Vol. 14, No. 6, pp. A1172. print.
Meeting Info.: Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society Seattle, Washington, USA May 12-16, 2000
ISSN: 0892-6638.
DT Conference
LA English
SL English
CC Immunology and Immunochemistry - General; Methods *34502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Animal *03506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae 86375
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis)
IT Diseases
autoimmune lymphoproliferative disorder: immune system disease
IT Chemicals & Biochemicals
forkhead family protein; **scurfy** gene product
IT Miscellaneous Descriptors
T cell activation; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
GEN mouse **sf** gene [mouse **scurfy** gene] (Muridae): mutation

L61 ANSWER 7 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:492037 BIOSIS
DN PREV200000492158
TI Mutations in the novel forkhead/winged-helix protein **scurfin** cause neonatal diabetes, enteropathy, thrombocytopenia, and endocrinopathy syndrome, the human equivalent of the **scurfy** mouse.
AU Wildin, R. S. (1); **Ramsdell, F.**; Peake, J.; Faravelli, F.; Casanova, J.-L.; Buist, N. (1); **Brunkow, M.**
CS (1) Molec. and Med. Genetics, Oregon Health Sci Univ, Portland, OR USA
SO American Journal of Human Genetics, (October, 2000) Vol. 67, No. 4 Supplement 2, pp. 41. print.
Meeting Info.: 50th Annual Meeting of the American Society of Human Genetics Philadelphia, Pennsylvania, USA October 03-07, 2000 American Society of Human Genetics
. ISSN: 0002-9297.
DT Conference
LA English
SL English
CC Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Human *03508
Biochemical Studies - General *10060

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Metabolism - Metabolic Disorders *13020
Digestive System - Physiology and Biochemistry *14004
Digestive System - Pathology *14006
Endocrine System - General *17002
Endocrine System - Pancreas *17008
Immunology and Immunochemistry - General; Methods *34502
BC Hominidae 86215
Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Molecular Genetics (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
CD8 positive T cells: immune system; Cd4 positive T cell: immune system; focal inflammatory cell: infiltration; intestinal mucosa: digestive system; pancreatic islets: endocrine system
IT Diseases
anemia: blood and lymphatic disease; diabetes: endocrine disease/pancreas, metabolic disease, neonatal presentation; endocrinopathy syndrome: endocrine disease; enteropathy: digestive system disease; growth retardation syndrome: X-linked recessive autoimmune disorder; thrombocytopenia: blood and lymphatic disease
IT Chemicals & Biochemicals
CpG dinucleotides; DIETER: phenotypes; DNA: binding activity; **scurfin**: mutations, novel forkhead/winged-helix protein
IT Alternate Indexing
Anemia (MeSH); Diabetes Mellitus (MeSH); Thrombocytopenia (MeSH)
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae); **scurfy** mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L61 ANSWER 8 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:201210 BIOSIS
DN PREV199800201210
TI The murine mutation **scurfy** (**sf**) produces a severe lymphoproliferative disease which is autoimmune in nature.
AU Zahorsky, J. L.; Wilkinson, J. E.
CS Dep. Pathobiol., Univ. Tenn. Coll. Vet. Med., P.O. Box 1071, Knoxville, TN 37901-1071 USA
SO FASEB Journal, (**March 17, 1998**) Vol. 12, No. 4, pp. A488.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part 1 San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology . ISSN: 0892-6638.
DT Conference
LA English
CC Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Genetics and Cytogenetics - Animal *03506
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520

BC Muridae 86375
IT Major Concepts
Genetics; Immune System (Chemical Coordination and Homeostasis)
IT Diseases
autoimmune lymphoproliferative disease: blood and lymphatic disease, immune system disease
IT Chemicals & Biochemicals
scurfy gene: mutation
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L61 ANSWER 9 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:107110 BIOSIS
DN PREV199698679245
TI Disease in the **scurfy** (**sf**) mouse is associated with overexpression of cytokine genes.
AU Kanangat, Sivadasan; Blair, Patrick; Reddy, Ramani; Deheshia, Massoud; Godfrey, Virginia; Rouse, Barry T.; Wilkinson, Erby (1)
CS (1) Dep. Pathol., Coll. Vet. Med., Univ. Tennessee, PO Box 1071, Knoxville, TN 37996 USA
SO European Journal of Immunology, (1996) Vol. 26, No. 1, pp. 161-165. ISSN: 0014-2980.
DT Article
LA English
AB The murine X-linked lymphoproliferative disease **scurfy** is similar to the Wiskott-Aldrich syndrome in humans. Disease in **scurfy** (**sf**) mice is mediated by CD4T cells. Based on similarities in **scurfy** mice and transgenic mice that overexpress specific cytokine genes, we evaluated the expression of cytokines in the lesions of **sf** mice by Northern blotting, quantitative reverse-transcription polymerase chain reaction (RT-PCR) and by hybridization in situ. Overall, the phenotypic characteristics of **scurfy** disease correlated well with increased interleukin (IL)-4 (lymphadenopathy), IL-6 (B cell proliferation, hypergammaglobulinemia), IL-7 (dermal inflammatory cell infiltration), and high levels of tumor necrosis factor-alpha (wasting).
CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Sex Differences *03510
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Biophysics - General Biophysical Techniques 10504
Enzymes - Methods 10804
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Developmental Biology - Embryology - Morphogenesis, General *25508
Immunology and Immunochemistry - General; Methods *34502
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae *86375
IT Major Concepts

Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Development; Genetics; Immune System (Chemical Coordination and Homeostasis); Methods and Techniques

IT Miscellaneous Descriptors
IN-SITU HYBRIDIZATION; MURINE X-LINKED LYMPHOPROLIFERATIVE DISEASE; NORTHERN BLOT; PHENOTYPE; QUANTITATIVE REVERSE-TRANSCRIPTION POLYMERASE CHAIN REACTION

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

L61 ANSWER 10 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:505040 BIOSIS
DN PREV199598510090
TI The mouse homolog of the Wiskott-Aldrich syndrome protein (WASP) gene is highly conserved and maps near the **scurfy** (**sf**) mutation on the X chromosome.
AU Derry, Jonathan M. J.; Wiedemann, Philipp; Blair, Patrick; Wang, Yuker; Kerns, Julie A.; Lemahieu, Vanessa; Godfrey, Virginia L.; Wilkinson, J. Erby; Francke, Uta (1)
CS (1) Howard Hughes Med. Inst., Stanford Univ. Med. Cent., Stanford, CA 94305-5428 USA
SO Genomics, (1995) Vol. 29, No. 2, pp. 471-477.
ISSN: 0888-7543.
DT Article
LA English
AB The mouse WASP gene, the homolog of the gene mutated in Wiskott-Aldrich syndrome, has been isolated and sequenced. The predicted amino acid sequence is 86% identical to the human WASP sequence. A distinct feature of the mouse gene is an expanded polymorphic GGA trinucleotide repeat that codes for polyglycine and varies from 15 to 17 triplets in different Mus musculus strains. The genomic structure of the mouse gene closely resembles the human with respect to exon-intron positions and intron lengths. The mouse WASP gene is expressed as an apprx 2.4-kb mRNA in thymus and spleen. Chromosomal mapping in an interspecific M. musculus/M. spretus backcross placed the Wasp locus near the centromere of the mouse X chromosome, inseparable from Gata1, Tcfe3, and **scurfy** (**sf**). This localization makes Wasp a candidate for involvement in **scurfy**, a T cell-mediated fatal lymphoreticular disease of mice that has previously been proposed as a mouse homolog of Wiskott-Aldrich syndrome. Northern analysis of **sf** tissue samples indicated the presence of WASP mRNA in liver and skin, presumably as a consequence of lymphocytic infiltration, but no abnormalities in the amount or size of mRNA present.
CC Evolution *01500
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Human *03508
Biophysics - Molecular Properties and Macromolecules *10506
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
BC Hominidae 86215
Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Evolution and Adaptation; Genetics; Hematology (Human

Medicine, Medical Sciences)
IT Sequence Data
amino acid sequence; molecular sequence data; nucleotide sequence
IT Miscellaneous Descriptors
BLEEDING; GENE MAPPING; HUMAN MODEL; LYMPHORETICULAR DISEASE; MOLECULAR EVOLUTION
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae); Mus musculus (Muridae); Mus spretus (Muridae)
ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates

L61 ANSWER 11 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:63215 BIOSIS
DN PREV199598077515
TI The mouse **scurfy** (**sf**) mutation is tightly linked to Gata1 and Tfe3 on the proximal X Chromosome.
AU Blair, P. J. (1); Carpenter, D. A.; Godfrey, V. L.; Russell, L. B.; Wilkinson, J. E.; Rinchik, E. M.
CS (1) Biol. Div., Oak Ridge Natl. Lab., PO Box 2009, Oak Ridge, TN 37831-8077 USA
SO Mammalian Genome, (1994) Vol. 5, No. 10, pp. 652-654.
ISSN: 0938-8990.
DT Article
LA English
CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Developmental Biology - Embryology - Descriptive Teratology and Teratogenesis *25552
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Development; Genetics
IT Miscellaneous Descriptors
CENTROMERIC REGION; GENOTYPE-PHENOTYPE RELATIONSHIP; LYMPHORETICULAR DISEASE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Mus musculus (Muridae); Mus spretus (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

L61 ANSWER 12 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:532774 BIOSIS
DN PREV199497545774
TI CD4+CD8- T cells are the effector cells in disease pathogenesis in the **scurfy** (**sf**) mouse.
AU Blair, Patrick J.; Bultman, Scott J.; Haas, Julia C.; Rouse, Barry T.; Wilkinson, J. Erby; Godfrey, Virginia L. (1)
CS (1) Biol. Div., Oak Ridge Natl. Lab., P.O. Box 2009, Oak Ridge, TN 37831-8077 USA
SO Journal of Immunology, (1994) Vol. 153, No. 8, pp. 3764-3774.
ISSN: 0022-1767.

DT Article
LA English
AB Mice hemizygous for the X-linked mutation, **scurfy** (**sf**), exhibit a fatal lymphoreticular disease that is mediated by T lymphocytes. To evaluate the respective roles of CD4 or CD8 single positive T cells in **scurfy** disease, neonates were treated with mAbs directed against the CD4 or CD8 molecules. Whereas mice treated with an anti-CD8 Ab developed lesions and succumbed to disease at the same time (17 days) as their untreated **scurfy** littermates, mice treated with an anti-CD4 Ab lived up to 11 wk before developing **scurfy** disease. To insure a more complete elimination of the T cell subsets, the **scurfy** mutation was bred onto beta-2-microglobulin (beta-2m)-deficient (CD8-less) and CD4-deficient transgenic mouse lines. Whereas there was little moderation of disease in beta-2m-deficient **scurfy** mice, CD4-deficient **scurfy** mice had markedly decreased **scurfy** lesions and a prolonged life span, similar to that of anti-CD4-treated **sf**/Y mice. Additionally, **scurfy** disease disease was transplanted into H-2-compatible nude mice through the adoptive transfer of CD4+CD8- T cells, but not CD4-CD8+ T cells. Flow-cytometric analysis revealed that **sf**/Y mice have an increased percentage of activated CD4+ T cells in their lymph nodes. In addition, there is an increase in the in vitro production of cytokines in the cultured splenocytes of CD8-less, but not CD4-less, **scurfy** mice. These data suggest that CD4+ T cells are critical mediators of disease in the **scurfy** mouse.
CC Cytology and Cytochemistry - Animal 02506
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Genetics; Immune System (Chemical Coordination and Homeostasis)
IT Miscellaneous Descriptors
CD4 POSITIVE T CELLS; CD8 NEGATIVE T CELLS; DISEASE PROGRESSION; FATAL LYMPHOPROLIFERATIVE DISEASE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

L61 ANSWER 13 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:431513 BIOSIS
DN PREV199497444513
TI Transplantation of T cell-mediated, lymphoreticular disease from the **scurfy** (**sf**) mouse.
AU Godfrey, Virginia L. (1); Rouse, Barry T.; Wilkinson, J. Erby
CS (1) Biol. Div., Oak Ridge National Lab., PO Box 2009, Oak Ridge, TN 37831-8077 USA
SO American Journal of Pathology, (1994) Vol. 145, No. 2, pp. 281-286. ISSN: 0002-9440.
DT Article
LA English
AB The X-linked mutation, **scurfy** (**sf**), causes a fatal

lymphoreticular disease characterized by runting, lymphadenopathy, splenomegaly, hypergammaglobulinemia, exfoliative dermatitis, Coombs'-positive anemia, and death by 24 days of age. T lymphocytes are required to mediate this syndrome as shown by a total absence of disease in mice bred to be **scurfy** and nude (**sf**/Y; nu/nu). The **scurfy** phenotype is not transmitted by **sf**/Y bone marrow transplants, though cells of **scurfy** origin do reconstitute all lymphoid organs in the recipient mouse. These data suggest that **scurfy** disease results from an abnormal T cell development process and not from an intrinsic stem cell defect. We therefore tested the ability of transplanted **scurfy** thymuses to transmit **scurfy** disease to congenic euthymic mice, to athymic (nude) mice, and to severe combined immunodeficiency (SCID) mice. Euthymic recipients of **sf**/Y thymic grafts remained clinically normal as did all SCID and nude recipients of normal thymus transplants. Morphological lesions similar to those found in **scurfy** mice occurred in all H-2-compatible nude and SCID recipients of **sf**/Y thymic grafts. Intraperitoneal injections of **scurfy** thymocytes, splenocytes, and lymph node cells also transmitted the **scurfy** phenotype to H-2-compatible nude mice and SCID mice. Our findings indicate that **scurfy** disease can be transmitted to T cell-deficient mice by engraftment of **scurfy** T cells, but that Pathogenic **scurfy** T cell activities can be inhibited (or prevented) in immunocompetent recipient mice.

CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Anatomy and Histology, General and Comparative - Experimental Anatomy *11104
Anatomy and Histology, General and Comparative - Regeneration and Transplantation *11107
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Coelomic Membranes; Mesenteries and Related Structures 18200
Routes of Immunization, Infection and Therapy 22100
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Muridae *86375

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Genetics; Immune System (Chemical Coordination and Homeostasis); Morphology; Physiology

IT Miscellaneous Descriptors
ATHYMIC MOUSE; EUTHYMIC MOUSE; INTRAPERITONEAL ADMINISTRATION; LYMPH NODE CELL; SEVERE COMBINED IMMUNODEFICIENCY MOUSE; SPLENOCYTE; THYMOCYTE; THYMUS

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

L61 ANSWER 14 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:243428 BIOSIS
DN PREV199497256428
TI CD4+8 T cells are the effector cells in disease pathogenesis in the **scurfy** (**sf**) mouse.
AU Blair, P. J. S. B. Bultman; Haas, J. C.; Rouse, B. T.; Wilkinson, J. E.; Godfrey, V. L.
CS Biol. Div., ORNL, Oak Ridge, TN 37831-8077 USA

SO FASEB Journal, (1994) Vol. 8, No. 4-5, pp. A902.
Meeting Info.: Experimental Biology 94, Parts I and II Anaheim, California, USA April 24-28, 1994
ISSN: 0892-6638.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Immune System (Chemical Coordination and Homeostasis)
IT Miscellaneous Descriptors
ANIMAL MODEL; MEETING ABSTRACT
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates

L61 ANSWER 15 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:184106 BIOSIS
DN PREV199395094556
TI Partial inversion of gene order within a homologous segment on the X chromosome.
AU Laval, Steven H.; Boyd, Yvonne (1)
CS (1) Genetics Div., Medical Res Council Radiobiol. Unit, Chilton, Didcot, Oxon OX11 ORD UK
SO Mammalian Genome, (1993) Vol. 4, No. 2, pp. 119-123.
ISSN: 0938-8990.
DT Article
LA English
AB The locus for the erthyroid transcription factor, GATA1, has been positioned in the small interval between DXS255 and TIMP on the proximal short arm of the human X Chromosome (Chr) by use of a partial human cDNA clone and a well-characterized somatic cell hybrid panel. Analysis of selected recombinants from 108 Mus musculus times Mus spretus backcross progeny with the same clone confirmed that the homologous murine locus (Gf-1) lies between Otc and the centromere of the mouse X Chr. These data imply that a partial inversion of gene order has occurred within the conserved segment that represents Xp21.1-Xp11.23 in human (CYBB-GATA1) anc the proximal 6 cM of the mouse X Chr (Gf-1-Timp). Furthermore, they indicate that the mouse mutant **scurfy** and the human genetic disorder Wiskott-Aldrich syndrome, which have been mapped to the same regions as GATA1/Gf-1 in both species, may indeed by homologous disorders.
CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Genetics; Metabolism

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Mus musculus (Muridae); Mus spretus (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

L61 ANSWER 16 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:94578 BIOSIS
DN PREV199395049774
TI Two-dimensional polyacrylamide gel electrophoretic characterization of proteins from organs of C3H mice expressing the **scurfy** (**sf**) genetic mutation during early and late stages of disease progression.
AU Selkirk, J. K. (1); Hite, M. C.; Godfrey, V.; Merrick, B. A.; He, C.; Griesemer, R. A.; Daluge, D. R.; Mansfield, B. K.
CS (1) NIEHS, 111 Alexander Dr., Research Triangle Park, N.C. 27709 USA
SO Applied and Theoretical Electrophoresis, (1992) Vol. 3, No. 2, pp. 97-107. ISSN: 0954-6642.
DT Article
LA English
AB **Scurfy** (**sf**), is an X-linked recessive lethal mutation that occurs spontaneously in the C3H mouse. The disease is characterized by lymphoid and hematopoietic dysfunction. Affected male are of mall stature and exhibit scaliness and crusting of the eyelids, ears, tail, and feed, marked splenomegaly, moderate hepatomegaly, enlarged lymph nodes, and atrophy of the thymus. The average lifespan of the affected hemizygous males (**sf**/y) is 24 +- 0.7 days. Total cellular proteins were extracted from pooled samples of thymus and spleen obtaine dfrom combined litters of mice. Tissue-specific protein profiles characteristic of either **sf** mutant or normal mice were analyzed by two dimensional polyacrylamide gel electrophoresis (2DPQGE) at different stages of the phenotypic expression of the **sf** mutations, to identify changes in protein pattern sthat might be associated with the progression of the disease. The resultant gels were silver stained, digitized, and analyzed, by image analysis utilizing a pipelined image processor connected to a host computer. t 14 +- 1 days of age, protein patterns from **sf** mutant and normal mice control orgns showed considerable homogeneity, although there were proteins identified unique to the **sf** mutant and to the normal controls. At 20 +- 1 days of age, the pattern differences between the **sf** mutant and normal control increased markedly. Differences were expressed as the percent of protein that were unique to either the **sf** mutant or the normal control from the total number of each type. The percent of proteins that increased or decreased in the three organs utilized in this study ranged between 21%-39% at 14 days and were between 25%-54% in 20 days. Differences in protein expression between the normal and **sf** mutant as the disorder progressed for each of the three tissues examined. In addition, thymus protein profiles from 9 day old littermates that were phenotypically normal but genotypically unknown were evaluated to determine if marker proteins could be identified for the **sf** mutation. Limited protein changes were noted at relative molecular weights of 66, 60, 54, 39, 37, 33, 25, 23, 27 and 11 kDa. These data suggest that the **sf** mutation follows a trackable pattern of protein expression and repression different than the normal control C3H mouse. Several potential marker proteins associated with the **sf** mutation were identified in 9 day thymus prior to the phenotypic expression of the disease. These putative biomarker smay be useful for characterizing the **sf** mutation and the mutant may act a possible model the Wiskott-Aldrich syndrome (WAS).
CC Genetics and Cytogenetics - Animal *03506
Biochemical Methods - Proteins, Peptides and Amino Acids *10054

Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Replication, Transcription, Translation *10300
Biophysics - General Biophysical Techniques *10504
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Developmental Biology - Embryology - Experimental *25504
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Development; Genetics; Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Chemicals & Biochemicals
POLYACRYLAMIDE
IT Miscellaneous Descriptors
ANALYTICAL METHOD; GENE EXPRESSION
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates
RN 9003-05-8 (POLYACRYLAMIDE)

L61 ANSWER 17 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1992:292846 BIOSIS
DN BR43:5196
TI FATAL LYMPHORETICULAR DISEASE IS ESTABLISHED EARLY IN THYMIC DEVELOPMENT IN THE **SCURFY SF** MOUSE.
AU BLAIR P; WILKINSON J E; GODFREY V L
CS BIOL. DVI., ORNL, OAK RIDGE, TENN. 37831-8077.
SO MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB) PART II, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM SOC EXP BIOL) J. (1992) 6 (5), A1700.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference
FS BR; OLD
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal 02506
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Sex Differences *03510
Pathology, General and Miscellaneous - Necrosis *12510
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Developmental Biology - Embryology - Pathological *25503
Developmental Biology - Embryology - Morphogenesis, General *25508
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT X-LINKED DISORDER

L61 ANSWER 18 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:383692 BIOSIS
DN BA92:61007
TI FATAL LYMPHORETICULAR DISEASE IN THE **SCURFY SF** MOUSE REQUIRES T CELLS THAT MATURE IN A **SF** THYMIC ENVIRONMENT POTENTIAL MODEL FOR THYMIC EDUCATION.
AU GODFREY V L; WILKINSON J E; RINCHIK E M; RUSSELL L B
CS BIOL. DIV., OAK RIDGE NATIONAL LAB., PO BOX 2009, OAK RIDGE, TENN.

37831-8077.
SO PROC NATL ACAD SCI U S A, (1991) 88 (13), 5528-5532.
CODEN: PNASA6. ISSN: 0027-8424.
FS BA; OLD
LA English
AB Characteristic lesions in mice hemi- or homozygous for the X-linked mutation **scurfy** (**sf**) include lymphohistocytic proliferation in the skin and lymphoid organs, Coombs' test-positive anemia, hypergammaglobulinemia, and death by 24 days of age. The role of thymus in the development of fatal lymphoreticular disease in the **scurfy** mouse was investigated. Neonatal thymectomy doubles the life span of **scurfy** mice, moderates the histologic lesions, and prevents anemia, despite the continued presence of high levels of serum IgG. Animals bred to be nude and **scurfy** (nu/nu; **sf**/Y) are viable, fertile, and free of **scurfy** lesions. Bone marrow from **scurfy** mice can reconstitute lethally irradiated, H-2-compatible animals but does not transmit **scurfy** disease. We conclude, from these data, that **scurfy** lesions are mediated by T lymphocytes that mature in an abnormal (**sf**) thymic environment.
CC Genetics and Cytogenetics - Animal *03506
Radiation - Radiation and Isotope Techniques *06504
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Anatomy and Histology, General and Comparative - Experimental Anatomy 11104
Anatomy and Histology, General and Comparative - Regeneration and Transplantation *11107
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Carbohydrates 13004
Metabolism - Minerals 13010
Metabolism - Proteins, Peptides and Amino Acids *13012
Blood, Blood-Forming Organs and Body Fluids - General; Methods 15001
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods 18001
Developmental Biology - Embryology - Morphogenesis, General 25508
Immunology and Immunochemistry - Immunopathology, Tissue Immunology 34508
BC Muridae 86375
IT Miscellaneous Descriptors
ABNORMAL MATURATION ANEMIA X-LINKED LYMPHORETICULAR DISEASE HYPERGAMMAGLOBULINEMIA BONE MARROW TRANSPLANT IRRADIATION NEONATAL THYMECTOMY

L61 ANSWER 19 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:364118 BIOSIS
DN BA92:52343
TI X-LINKED LYMPHORETICULAR DISEASE IN THE **SCURFY SF** MUTANT MOUSE.
AU GODFREY V L; WILKINSON J E; RUSSELL L B
CS BIOL. DIV., ORNL, P.O. BOX 2009, OAK RIDGE, TENN. 37831-8077.
SO AM J PATHOL, (1991) 138 (6), 1379-1388.
CODEN: AJPAA4. ISSN: 0002-9440.
FS BA; OLD
LA English
AB **Scurfy** (**sf**) is a spontaneous, sex-linked, recessive mutation that maps to the extreme proximal portion of the X chromosome, about 2 centimorgans from sparse fur (spf). Hemizygotes for **sf** manifest several clinical disorders, evident at 14 days of age, including scaliness and crusting of the eyelids, ears, and tail, runting, reddening

and swelling of the genital papilla, anemia, cachexia, and early death (average, 24 days). Our studies indicate that the phenotype of hemizygous **scurfy** is not, as has been suggested, a model for human X-linked ichthyosis, but appears to be a disease primarily affecting the lymphoreticular, and possibly the hematopoietic, systems. Gross lesions include marked splenomegaly, hepatomegaly, enlarged lymph nodes, and variable thickening of the ears. The characteristic histologic lesion is a lymphohistiocytic proliferation and infiltration of peripheral lymph nodes, spleen, liver, and skin. In routine hematoxylin and eosin-stained sections, these lesions efface lymph node architecture, thicken the dermis, and form nodular portal infiltrates in the liver. **Scurfy** lesions characteristically contain a population of large blastlike cells with round to oval nuclei, a vesicular chromatin pattern, and prominent single nucleoli. Mixed perivascular infiltrates of lymphocytes, macrophages, and granulocytes sometimes are found in kidney, heart, pancreas, lung, and mesenteries. There is excessive hematopoiesis in the liver and spleen. Cells expressing B220 or Thy-1 antigens localize to appropriate areas in the lymph nodes and spleen, but are rare in the portal infiltrates and are absent from the skin. There is a marked, polyclonal increase in serum IgG, severe Coombs'-positive anemia, and leukocytosis with atypical mononuclear cells. **Scurfy** mice are negative for antinuclear antibodies. Despite their morphologically aberrant lymphoreticular system, **scurfy** mice can exist in a conventional environment without evidence of opportunistic infection. Raising **scurfy** mice in a specific-pathogen-free environment does not alter disease expression. Thus, while our findings indicate that **scurfy** disease may be the result of immune dysfunction, it is not a classic immunodeficiency.

CC Microscopy Techniques - Histology and Histochemistry 01056
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Sex Differences *03510
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Muridae 86375

IT Miscellaneous Descriptors
LYMPHOHISTIOCYTIC PROLIFERATION IMMUNE DYSFUNCTION SEX-LINKED RECESSIVE MUTATION PATHOGENESIS

L61 ANSWER 20 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:331687 BIOSIS
DN BR41:28237
TI DOES THE **SCURFY** MUTATION CAUSE A DEFECT IN THE THYMIC MICROENVIRONMENT?.
AU BLAIR P; GODFREY V L; WILKINSON J E
CS BIOL. DIV., ORNL, OAK RIDGE, TENN. 37831-8077.
SO 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J. (1991) 5 (6), A1701.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference
FS BR; OLD
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Anatomy and Histology, General and Comparative - Experimental Anatomy 11104
Anatomy and Histology, General and Comparative - Regeneration and

Transplantation *11107
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System - Thymus *17016
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT MOUSE T CELL TRANSPLANTATION

L61 ANSWER 21 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:331686 BIOSIS
DN BR41:28236
TI THYMUS TRANSPLANT TRANSMISSION OF **SCURFY** MOUSE LYMPHORETICULAR DISEASE IS H-2 RESTRICTED.
AU GODFREY V L; COLLIER J; WILKENSON J E
CS BIOL. DIV., ORNL, OAK RIDGE, TENN. 37831-8077.
SO 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J. (1991) 5 (6), A1701.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference
FS BR; OLD
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Sex Differences *03510
Anatomy and Histology, General and Comparative - Experimental Anatomy 11104
Anatomy and Histology, General and Comparative - Regeneration and Transplantation *11107
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System - Thymus *17016
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT X-LINKED RECESSIVE MUTATION T-CELL

L61 ANSWER 22 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:438575 BIOSIS
DN BR39:86436
TI **SCURFY** MUTANT MICE SHOW HEMATOLOGICAL ABNORMALITIES RESEMBLING THOSE IN WISKOTT-ALDRICH SYNDROME.
AU LYON M F; PETERS J; GLENISTER P H; BALL S; WRIGHT E
CS M.R.C. RADIOBIOL. UNIT, CHILTON, DIDCOT, OXON OX11 0RD.
SO SYMPOSIUM ON MAMMALIAN GENETICS, LONDON, ENGLAND, UK, NOVEMBER 7-8, 1989. GENET RES. (1990) 55 (2), 129.
CODEN: GENRA8. ISSN: 0016-6723.
DT Conference
FS BR; OLD
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Pathology, General and Miscellaneous - Necrosis *12510

Digestive System - Pathology *14006
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Integumentary System - Pathology *18506
Developmental Biology - Embryology - Pathological *25503
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT X-CHROMOSOME SCALY SKIN DIARRHEA EARLY DEATH IMMUNODEFICIENCY

L61 ANSWER 23 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:324155 BIOSIS
DN BR39:31491
TI THE **SCURFY** MOUSE POTENTIAL MODEL FOR THYMIC EDUCATION.
AU GODFREY V L; WILKINSON J E; RUSSELL L B
CS BIOL. DIV., ORNL, OAK RIDGE, TENN. 37831-8077.
SO JOINT MEETING OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY AND THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS, NEW ORLEANS, LOUISIANA, USA, JUNE 4-7, 1990. FASEB (FED AM SOC EXP BIOL) J. (1990) 4 (7), A1727.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference
FS BR; OLD
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Genetics and Cytogenetics - Animal *03506
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Developmental Biology - Embryology - Experimental *25504
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT GENETICS T-CELL ENVIRONMENT LYMPHOPROLIFERATIVE DISEASE

L61 ANSWER 24 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:239195 BIOSIS
DN BA89:126148
TI THE **SCURFY** MOUSE MUTANT HAS PREVIOUSLY UNRECOGNIZED HEMATOLOGICAL ABNORMALITIES AND RESEMBLES WISKOTT-ALDRICH SYNDROME.
AU LYON M F; PETERS J; GLENISTER P H; BALL S; WRIGHT E
CS MED. RES. COUNCIL RADIOBIOL. UNIT, CHILTON, DIDCOT, OXON OX11 ORD, UK.
SO PROC NATL ACAD SCI U S A, (1990) 87 (7), 2433-2437.
CODEN: PNASA6. ISSN: 0027-8424.
FS BA; OLD
LA English
AB The X chromosome-linked **scurfy** (**sf**) mutant of the mouse is recognized by the scaliness of the skin from which the name is derived and results in death of affected males at about 3-4 weeks of age. Consideration of known man-mouse homologies of the X chromosome prompted hematological studies, which have shown that the blood is highly abnormal. The platelet and erythrocyte counts are both reduced and become progressively lower relative to normal as the disease progresses. There is gastrointestinal bleeding, and most animals appear to die of severe anemia. By contrast, the leukocyte count is consistnetly raised. Some animals showed signs of infection but it is not yet clear whether there is immunodeficiency. Other features include the scaly skin and apparently

reduced lateral growth of the skin, conjunctivitis, and diarrhea in some animals. The mutant resembles Wiskott-Aldrich syndrome in man, which is characterized by thrombocytopenia, eczema, diarrhea, and immunodeficiency. The loci of the human and mouse genes lie in homologous segments of the X chromsome, although apparently in somewhat different positions relative to other gene loci. **Scurfy** differs from Wiskott-Aldrich syndrome in that **scurfy** males are consistently hypogonadal.

CC Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Human *03508
Blood, Blood-Forming Organs and Body Fluids - General; Methods 15001
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Reproductive System - Pathology *16506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Hominidae 86215
Muridae 86375

IT Miscellaneous Descriptors
HUMAN X CHROMOSOME ANEMIA IMMUNODEFICIENCY THROMBOCYTOPENIA HYPOGONADISM

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L78 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:26877 HCAPLUS
DN 134:221325
TI Disruption of a new forkhead/winged-helix protein, **scurfin**, results in the fatal lymphoproliferative disorder of the **scurfy** mouse
AU Brunkow, Mary E.; Jeffery, Eric W.; Hjerrild, Kathryn A.; Paeper, Bryan; Clark, Lisa B.; Yasayko, Sue-Ann; Wilkinson, J. Erby; Galas, David; Ziegler, Steven F.; Ramsdell, Fred

CS Celltech Chiroscience, Inc., Bothell, WA, USA
SO Nature Genetics (2001), 27(1), 68-73
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America Inc.
DT Journal
LA English
CC 15-8 (Immunochemistry)
Section cross-reference(s): 3
AB **Scurfy** (**sf**) is an X-linked recessive mouse mutant resulting in lethality in hemizygous males 16-25 days after birth, and is characterized by overproliferation of CD4+CD8- T lymphocytes, extensive multiorgan infiltration and elevation of numerous cytokines. Similar to animals that lack expression of either Ctla-4 or Tgf-.beta., the pathol. obsd. in **sf** mice seems to result from an inability to properly regulate CD4+CD8- T-cell activity. Here the authors identify the gene defective in **sf** mice by combining high-resoln. genetic and phys. mapping with large-scale sequence anal. The protein encoded by this gene (designated **Foxp3**) is a new member of the forkhead/winged-helix family of transcriptional regulators and is highly conserved in humans. In **sf** mice, a frameshift mutation results in a product lacking the forkhead domain. Genetic complementation demonstrates that the protein product of **Foxp3**, **scurfin**, is essential for normal immune homeostasis.
ST forkhead winged helix protein **scurfin** fatal lymphoproliferative disorder **scurfy**; sequence **scurfin** cDNA gene mouse human; **scurfy** mouse fatal lymphoproliferative disorder **scurfin** mutation
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**Foxp3**; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GATA-binding protein 1, gene sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human and)
IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(Gata1; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human and)
IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(Pim2, sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human and)
IT CD4-positive T cell
DNA sequences
Lymphoproliferative disorders
Mouse (Mus musculus)
Protein sequences
cDNA sequences
(disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy**

mouse, in relation to genomic and cDNA sequences of mouse and human)

IT Protein motifs
(forkhead/winged-helix; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT Mutation
(frameshift; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(gene Pim2, gene sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human and)

IT Chromosome
(mouse X; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT Genetic mapping
(phys.; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT New natural products
(**scurfin** (protein))

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**scurfin**; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT **259851-63-3**, Protein (mouse gene **Fkhsf**)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT **259851-62-2**, Protein (human gene **Fkhsf**)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT 317312-88-2, GenBank AF277994
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT **259851-61-1**, GenBank AF277993 317312-86-0, GenBank AF277991
317312-87-1, GenBank AF277992

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human)

IT 320710-21-2, GenBank AF318279 320710-22-3, GenBank AF318280
320710-23-4, GenBank AF318281
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human and)

IT 317783-80-5, GenBank AF277995 317783-81-6, GenBank AF277996
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; disruption of new forkhead/winged-helix protein, **scurfin**, results in fatal lymphoproliferative disorder of **scurfy** mouse, in relation to genomic and cDNA sequences of mouse and human and)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L78 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:133832 HCAPLUS
DN 132:190512
TI Gene causing the mouse **scurfy** phenotype and its human ortholog
IN Brunkow, Mary E.; Jeffery, Eric W.; Hjerrild, Kathryn A.; Ramsdell, Fred
PA Darwin Discovery Ltd., UK
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2

DT Patent
LA English
IC ICM C12N015-12
ICS C07K014-47; C07K016-18; A61K038-17; C12Q001-68; G01N033-50; C12N015-63
CC **3-3** (Biochemical Genetics)
Section cross-reference(s): 6, 14, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000009693	A2	20000224	WO 1999-US18407	19990811	<--
	WO 2000009693	A3	20000615			
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	AU 9955594	A1	20000306	AU 1999-55594	19990811	<--
	EP 1105479	A2	20010613	EP 1999-942154	19990811	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	US 6414129	B1	20020702	US 1999-372668	19990811	<--
PRAI	US 1998-96195P	P	19980811	<--		
	WO 1999-US18407	W	19990811			

AB The present invention relates generally to the discovery of novel genes which, when mutated, results in a profound lymphoproliferative disorder. In particular, a mutant mouse designated **Scurfy** was used to identify the gene responsible for this disorder through backcross anal., phys. mapping, and large-scale sequencing. Isolated nucleic acid mols. are provided which encode **Fkhsf**, as well as mutant forms, which belongs to a family of related genes, all contg. a winged-helix DNA binding domain. The mouse **Fkhsf** gene spans .apprx.14 kb and contains 11 coding exons; the cDNA spans a coding region of 1287 bp and encodes a protein of 429 amino acids. The human ortholog to mouse **Fkhsf** cDNA is also provided. Also provided are expression vectors suitable for expressing such nucleic acid mols., and host cells contg. such expression vectors. Utilizing assays based upon the nucleic acid sequences disclosed herein (as well as mutant forms thereof), numerous mols. may be identified which modulate the immune system.

ST **scurfy** lymphoproliferative disease gene Fkh protein sequence
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Fkhsf**; gene causing the mouse **scurfy** phenotype and its human ortholog)
IT PCR (polymerase chain reaction)
(RT-PCR (reverse transcription-PCR); gene causing the mouse **scurfy** phenotype and its human ortholog)
IT cDNA sequences
(for **Fkhsf** gene causing the mouse **scurfy** phenotype and its human ortholog)
IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene **Fkhsf**; gene causing the mouse **scurfy** phenotype and its human ortholog)
IT Gene therapy
Immunoassay
Lymphoproliferative disorders

Molecular cloning
Mouse
Nucleic acid hybridization
Plasmid vectors
Retroviral vectors
Virus vectors
(gene causing the mouse **scurfy** phenotype and its human ortholog)

IT Antibodies
Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene causing the mouse **scurfy** phenotype and its human ortholog)

IT Hematopoietic precursor cell
T cell (lymphocyte)
(gene therapy with; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT Protein sequences
(of gene **Fkhsf** protein causing the mouse **scurfy** phenotype and its human ortholog)

IT Animal
Cat (Felis catus)
Dog (Canis familiaris)
Monkey
Rat
(transgenic; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT Adeno-associated virus
Alphavirus
Human adenovirus
Human herpesvirus
(vector; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT **259851-62-2**, Protein (human gene **Fkhsf**)
259851-63-3, Protein (mouse gene **Fkhsf**)
RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT **259851-60-0 259851-61-1**
RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT 259851-66-6, 24: PN: WO0009693 PAGE: 34 unclaimed DNA 259851-67-7, 25: PN: WO0009693 PAGE: 34 unclaimed DNA 259851-68-8, 26: PN: WO0009693 PAGE: 34 unclaimed DNA 259851-69-9, 27: PN: WO0009693 PAGE: 34 unclaimed DNA 259851-70-2, 28: PN: WO0009693 PAGE: 35 unclaimed DNA 259851-71-3, 29: PN: WO0009693 PAGE: 35 unclaimed DNA 259851-72-4, 30: PN: WO0009693 PAGE: 35 unclaimed DNA 259851-73-5, 31: PN: WO0009693 PAGE: 35 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; gene causing the mouse **scurfy** phenotype and its human ortholog)

IT 259144-26-8 259851-74-6

RL: PRP (Properties)
(unclaimed sequence; gene causing the mouse **scurfy** phenotype and its human ortholog)

L78 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:469282 HCAPLUS
DN 127:186234
TI A PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani
AU McKay, Gareth J.; Cooke, Louise R.
CS Department of Applied Plant Science, The Queen's University of Belfast, Agriculture and Food Science Centre, Newforge Lane, Belfast, BT9 5PX, UK
SO FEMS Microbiology Letters (**1997**), 152(2), 371-378
CODEN: FMLED7; ISSN: 0378-1097
PB Elsevier
DT Journal
LA English
CC **3-1** (Biochemical Genetics)
Section cross-reference(s): 10
AB Control of Helminthosporium solani, the cause of silver **scurf** in potato tubers, has been impaired by selection of benzimidazole-resistant strains as a result of repeated use of the fungicide thiabendazole. Identification of thiabendazole-resistant strains of H. solani by conventional techniques takes several weeks. Primers designed from conserved regions of the fungal .beta.-tubulin gene were used to PCR amplify and sequence a portion of the gene. A point mutation was detected at codon 198 in thiabendazole-resistant isolates causing a change in the amino acid sequence from glutamic acid to alanine or glutamine. Species-specific PCR primers designed to amplify this region were used in conjunction with a restriction endonuclease to cause cleavage in sensitive isolates only and thus provide a rapid diagnostic test to differentiate field isolates.
ST benzimidazole thiabendazole resistance mutation detection Helminthosporium; PCR detection benzimidazole thiabendazole resistance Helminthosporium
IT DNA sequences
Helminthosporium solani
PCR (polymerase chain reaction)
Protein sequences
(PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT Gene, microbial
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(for .beta.-tubulin; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT Mutation
(point, codon 198 Glu to Ala/Gln; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT Tubulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(.beta.-; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194370-47-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194465-74-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)

IT 194372-49-1
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer SS-for; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-50-4
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer SS-rev; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-43-5
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer .beta.-tubf1; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-44-6
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer .beta.-tubf2; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-45-7
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer .beta.-tubf3; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-46-8
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer .beta.-tubr1; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-47-9
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer .beta.-tubr2; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 194372-48-0
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(primer .beta.-tubr3; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 51-17-2, 1H-Benzimidazole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)
IT 148-79-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; PCR-based method to characterize and identify benzimidazole resistance in Helminthosporium solani)

L78 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:706254 HCAPLUS
DN 126:2200
TI Long-range map of a 3.5-Mb region in Xp11.23-22 with a sequence-ready map from a 1.1-Mb gene-rich interval
AU Schindelhauer, Dirk; Hellebrand, Heide; Grimm, Lena; Bader, Ingrid; Meitinger, Thomas; Wehnert, Manfred; Ross, Mark; Meindl, Alfons
CS Abteilung fur Padiatrische Genetik, Kinderpoliklinik der Universitat Munchen, Munchen, 80336, Germany
SO Genome Research (**1996**), 6(11), 1056-1069
CODEN: GEREFS; ISSN: 1088-9051
PB Cold Spring Harbor Laboratory Press
DT Journal

LA English
CC **3-3** (Biochemical Genetics)
Section cross-reference(s): 13
AB Most of the yeast artificial chromosomes (YACs) isolated from the Xp11.23-22 region have shown instability and chimerism and are not a reliable resource for detg. phys. distances. The authors therefore constructed a long-range pulsed-field gel electrophoresis map that encompasses ~3.5 Mb of genomic DNA between the loci TIMP and DXS146 including a CpG-rich region around th eWASP and TFE-3 gene loci. A combined YAC-cosmid contig was constructed along the genomic map and was used for fine-mapping of 15 polymorphic microsatellites and 30 expressed sequence tags (ESTs) or sequence transcribed sites (STSs), (HB3-OATL1pseudogenes-DXS6950)-DXS6949-DXS6941-DXS7464E(MG61)-GW1E(EBP)-DXS7927E(MG81)-RBM-DXS722-DXS7467E(MG21)-DXS1011E-WASP-DXS6940-DXS73466E(MG44)-GF1-DXS226-DXS1126-DXS1240-HB1-DXS7469E-(DXS6665-DXS1470)-TFE3-DXS7468E-SYP-DXS1208-HB2E-DXS573-DXS1331-DXS6666-DXS1039-DXS1426-DXS1416-DXS7647-DXS8222-DXS6850-DXS255-CIC-5-DXS146-cen. A sequence-ready map was constructed for an 1100-kb gene-rich interval flanked by the markers HB3 and DXS1039, from which six novel ESTs/STSs were isolated, thus increasing the no. of markers used in this interval to thirty. This precise ordering is a prerequisite for the construction of a transcription map of this region that contains numerous disease loci, including those for several forms of retinal degeneration and mental retardation. In addn., the map provides the base to delineate the corresponding syntenic region in the mouse, where the mutants **scurfy** and tattered are localized.
ST human map chromosome X T54 cDNA; EST STS map chromosome X human; restriction YAC MAP chromosome X human
IT Genetic element
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(CpG island, assocd. with gene; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(T54; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT Proteins, specific or class
RL: PRP (Properties)
(T54; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT Chromosome
(human X, Xp11.23-22; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT Protein sequences
cDNA sequences
(long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT EST (expressed sequence tag)
Genetic markers
Microsatellite DNA
STS (sequence-tagged site)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT Genetic mapping
(restriction, combination of YAC and restriction; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)
IT 184012-91-7, Protein T54 (human 378-amino acid)
RL: PRP (Properties)

(amino acid sequence; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)

IT 183100-19-8, Genbank U66359
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; long-range map of 3.5-Mb region in Xp11.23-22 with sequence-ready map from 1.1-Mb gene-rich interval)

L78 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:880635 HCAPLUS
DN 124:22898
TI The mouse homolog of the Wiskott-Aldrich syndrome protein (WASP) gene is highly conserved and maps near the **scurfy** (**sf**) mutation on the X chromosome
AU Derry, Jonathan M. J.; Wiedemann, Philipp; Blair, Patrick; Wang, Yuker; Kerns, Julie A.; Lemahieu, Vanessa; Godfrey, Virginia L.; Wilkinson, J. Erby; Francke, Uta
CS Howard Hughes Medical Institute, Stanford University Medical Center, Stanford, CA, 94305, USA
SO Genomics (**1995**), 29(2), 471-77
CODEN: GNMCEP; ISSN: 0888-7543
PB Academic
DT Journal
LA English
CC **3-3** (Biochemical Genetics)
Section cross-reference(s): 14
AB The mouse WASP gene, the homolog of the gene mutated in Wiskott-Aldrich syndrome, has been isolated and sequenced. The predicted amino acid sequence is 86% identical to the human WASP sequence. A distinct feature of the mouse gene is an expanded polymorphic GGA trinucleotide repeat that codes for polyglycine and varies from 15 to 17 triplets in different Mus musculus strains. The genomic structure of the mouse gene closely resembles the human with respect to exon-intron positions and intron lengths. The mouse WASP gene is expressed as an .apprx.2.4-kb mRNA in thymus and spleen. Chromosomal mapping in an interspecific M. musculus/M. spretus backcross placed the Wasp locus near the centromere of the mouse X chromosome, inseparable from Gata1, Tcfe3, and **scurfy** (**sf**). This localization makes Wasp a candidate for involvement in **scurfy**, a T cell-mediated fatal lymphoreticular disease of mice that has previously been proposed as a mouse homolog of Wiskott-Aldrich syndrome. Northern anal. of **sf** tissue samples indicated the presence of WASP mRNA in liver and skin, presumably as a consequence of lymphocytic infiltration, but no abnormalities in the amt. or size of mRNA present.
ST Wiskott Aldrich syndrome mouse protein sequence; WASP gene protein mouse **scurfy** mutation
IT Gene, animal
RL: PRP (Properties)
(WASP; mouse homolog of Wiskott-Aldrich syndrome protein gene is highly conserved and maps near **scurfy** (**sf**) mutation on X chromosome)
IT Spleen
Thymus gland
(mouse WASP gene mRNA expression in thymus and spleen)
IT Aldrich syndrome
Mouse
(mouse homolog of Wiskott-Aldrich syndrome protein gene is highly conserved and maps near **scurfy** (**sf**) mutation on X chromosome)
IT Deoxyribonucleic acid sequences
(of mouse WASP gene 5'-flank)
IT Protein sequences
(of mouse WASP gene protein)

IT Mutation
(**scurfy** (**sf**); mouse WASP gene mRNA expression in thymus and spleen)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**scurfy**; mouse homolog of Wiskott-Aldrich syndrome protein gene is highly conserved and maps near **scurfy** (**sf**) mutation on X chromosome)
IT Deoxyribonucleic acid sequences
(complementary, for mouse WASP gene protein)
IT Chromosome
(mouse X, mouse homolog of Wiskott-Aldrich syndrome protein gene is highly conserved and maps near **scurfy** (**sf**) mutation on X chromosome)
IT 171546-20-6, Protein (mouse clone MW1 WASP gene)
RL: PRP (Properties)
(amino acid sequence; mouse WASP gene mRNA expression in thymus and spleen)
IT 171546-19-3 171546-21-7
RL: PRP (Properties)
(nucleotide sequence; mouse WASP gene mRNA expression in thymus and spleen)

L78 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:201987 HCAPLUS
DN 123:75916
TI The mouse **scurfy** (**sf**) mutation is tightly linked to Gata1 and Tfe3 on the proximal X chromosome
AU Blair, P. J.; Carpenter, D. A.; Godfrey, V. L.; Russell, L. B.; Wilkinson, J. E.; Rinchik, E. M.
CS Oak Ridge Graduate Program Biomedical Science, University Tennessee, Oak Ridge, TN, 37831-8077, USA
SO Mamm. Genome (**1994**), 5(10), 652-4
CODEN: MAMGEC; ISSN: 0938-8990
DT Journal
LA English
CC **3-3** (Biochemical Genetics)
Section cross-reference(s): 13, 14
AB The X-linked recessive mutation **scurfy** (**sf**) results in rapidly fatal lymphoreticular disease. An interspecific Mus musculus/ Mus spretus backcross segregating the **sf** mutation was used to map **sf** relative to other loci on the proximal X chromosome. Tight linkage of **sf** to both Gata1 and Tfe3 suggests that these genes may serve as mol. access points for ultimately identifying the **sf** locus.
ST gene **scurfy** Gata1 Tfe3 chromosome X
IT Gene, animal
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(Gata1; mouse **scurfy** (**sf**) mutation is tightly linked to Gata1 and Tfe3 on proximal X chromosome)
IT Genetic mapping
(mouse **scurfy** (**sf**) mutation is tightly linked to Gata1 and Tfe3 on proximal X chromosome)
IT Gene, animal
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**scurfy**; mouse **scurfy** (**sf**) mutation is tightly linked to Gata1 and Tfe3 on proximal X chromosome)
IT Gene, animal
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(TFE3, mouse **scurfy** (**sf**) mutation is tightly linked

to Gata1 and Tfe3 on proximal X chromosome)
IT Reticuloendothelial system
(lymphoreticular cell, disease; mouse **scurfy** (**sf**)
mutation is tightly linked to Gata1 and Tfe3 on proximal X chromosome)
IT Chromosome
(mouse X, mouse **scurfy** (**sf**) mutation is tightly
linked to Gata1 and Tfe3 on proximal X chromosome)

L78 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:249074 HCAPLUS
DN 118:249074
TI Partial inversion of gene order within a homologous segment on the X chromosome
AU Laval, Steven H.; Boyd, Yvonne
CS Radiobiol. Unit, Med. Res. Counc., Chilton/Didcot/Oxon, OX11 ORD, UK
SO Mamm. Genome (**1993**), 4(2), 119-23
CODEN: MAMGEC; ISSN: 0938-8990
DT Journal
LA English
CC **3-3** (Biochemical Genetics)
Section cross-reference(s): 13, 14
AB The locus for the erythroid transcription factor, GATA1, was positioned in the small interval between DXS255 and TIMP in the proximal short arm of the human X chromosome (Chr) by use of a partial human cDNA clone and a well-characterized somatic cell hybrid panel. Anal. of selected recombinants from 108 Mus musculus .times. Mus spretus backcross progeny with the same clone confirmed that the homologous murine locus (Gf-1) lies between Otc and the centromere of the mouse X Chr. These data imply that a partial inversion of gene order has occurred within the conserved segment that represents Xp21.1-Xp11.23 in human (CYBB-GATA1) and the proximal 6 cM of the mouse X Chr (Gf-1-Timp). Furthermore, they indicate that the mouse mutant **scurfy** and the human genetic disorder Wiskott-Aldrich syndrome, which have been mapped to the same regions as GATA1/Gf-1 in both species, may indeed be homologous disorders.
ST transcription factor GATA1 gene mapping; mouse gene Gf1 mapping; human gene GATA1 mapping; Wiskott Aldrich syndrome mouse human
IT Aldrich syndrome
(mouse mutant **scurfy** homologous to, transcription factor GATA1 gene mapping in relation to)
IT Genetic mapping
(of transcription factor GATA1 gene, on human and mouse X chromosomes)
IT Mouse
(transcription factor GATA1 gene Gf-1 of, mapping of)
IT Gene, animal
RL: BIOL (Biological study)
(GATA1, for transcription factor GATA1, mapping on human chromosome X of)
IT Gene, animal
RL: BIOL (Biological study)
(Gf-1, for transcription factor GATA1, mapping on mouse chromosome X of)
IT Ribonucleic acid formation factors
RL: BIOL (Biological study)
(GATA-1, gene for, mapping of, on human and mouse X chromosomes)
IT Chromosome
(human X, transcription factor GATA1 gene mapping on)
IT Chromosome
(mouse X, transcription factor GATA1 gene mapping on)

L78 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1983:570552 HCAPLUS
DN 99:170552
TI Steroid sulfatase in the mouse

AU Lam, S. T. S.; Polani, P. E.; Fensom, A. H.
CS Med. Sch., Guy's Hosp., London, SE1 9RT, UK
SO Genet. Res. (**1983**), 41(3), 299-302
CODEN: GENRA8; ISSN: 0016-6723
DT Journal
LA English
CC **3-3** (Biochemical Genetics)
Section cross-reference(s): 13, 14
AB A form of the human skin disease ichthyosis results from a mutation at the steroid sulfatase (EC 3.1.6.2) (STS) [9025-62-1] locus (STS) on the X chromosome. This locus appears to escape inactivation in the XX female, resulting in the expression of 2 doses of STS. The **scurfy** mutation in the mouse is thought to be homologous to the human disease and so should also be due to an STS deficiency. In male and female mice, in contrast to the human, the STS locus is subject to X chromosome inactivation. However, another interpretation of the results is possible, namely that STS may be coded for by an autosomal gene.
ST steroid sulfatase locus mouse genetics; ichthyosis steroid sulfatase mouse genetics
IT Mouse
(steroid sulfatase gene linkage to scrufy trait in)
IT Sex
(steroid sulfatase of fibroblasts and liver of adult and fetal mouse in relation to)
IT Mouse
(steroid sulfatase of fibroblasts and liver of adult and fetus of, genetics and ichthyosis and sex in relation to)
IT Liver, composition
(steroid sulfatase of, of adult and fetal mouse, genetics and ichthyosis and sex in relation to)
IT Fibroblast
(steroid sulfatase of, of fetal mouse, genetics and ichthyosis and sex in relation to)
IT Embryo
(fetus, steroid sulfatase of fibroblasts and liver of, of mouse, genetics and ichthyosis and sex in relation to)
IT Skin, disease or disorder
(ichthyosis, steroid sulfatase gene linkage of mouse in relation to)
IT Chromosome
(mouse X, inactivation of, steroid sulfatase of fibroblasts and liver of adult and fetal mouse in relation to)
IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(STS, for steroid sulfatase of mouse, linkage of, ichthyosis in relation to)
IT 9025-62-1
RL: PRP (Properties)
(of fibroblasts and liver, of adult and fetal mice, genetics and ichthyosis and sex in relation to)
IT 9025-35-8
RL: PRP (Properties)
(of fibroblasts and liver, of adult and fetal mice, steroid sulfatase genetics in relation to)

=> fil reg
FILE 'REGISTRY' ENTERED AT 07:19:22 ON 16 AUG 2002

STRUCTURE FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0
DICTIONARY FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0

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http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot l76

L76 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 259851-63-3 REGISTRY
CN **Protein (mouse gene Fkhsf) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO0009693 FIG: 2 claimed protein
CN GenBank AF277991-derived protein GI 12407637
CN GenBank AF277992-derived protein GI 12407639
CN Scurfin (Mus musculus gene Foxp3 alternatively spliced isoform)
CN Scurfin (Mus musculus gene Foxp3)
CN Transcription factor scurfin (mouse gene Foxp3 alternatively spliced isoform)
CN Transcription factor scurfin (mouse gene Foxp3)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:221325

REFERENCE 2: 132:190512

L76 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 259851-62-2 REGISTRY
CN **Protein (human gene Fkhsf) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: WO0009693 FIG: 4 claimed protein
CN GenBank AF277993-derived protein GI 12407641
CN Scurfin (human gene FOXP3)
CN Transcription factor scurfin (human gene FOXP3)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:221325

REFERENCE 2: 132:190512

L76 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 259851-61-1 REGISTRY
CN **DNA (human gene Fkhsf protein cDNA plus flanks) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: WO0009693 FIG: 3 claimed DNA
CN DNA (human gene FOXP3 scurfin cDNA plus flanks)
CN DNA (human gene FOXP3 transcription factor scurfin cDNA plus flanks)
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:221325

REFERENCE 2: 132:190512

L76 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN 259851-60-0 REGISTRY
CN **DNA (mouse gene Fkhsf protein cDNA plus flanks) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0009693 FIG: 1 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:190512

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FILE 'WPIX' ENTERED AT 07:21:36 ON 16 AUG 2002
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MOST RECENT DERWENT UPDATE 200252 <200252/DW>
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GUIDES, PLEASE VISIT:
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L84 ANSWER 1 OF 2 WPIX (C) 2002 THOMSON DERWENT
AN 2002-292072 [33] WPIX
DNC C2002-085818
TI Detecting mutations of human orthologs of murine scurfy gene, **FOXP3** for diagnosing **FOXP3** gene-related diseases in humans, by amplifying **FOXP3** nucleic acid sequence using oligonucleotide primers and detecting mutations.
DC B04 D16
IN BRUNKOW, M E
PA (CELL-N) CELLTECH R & D INC
CYC 97
PI WO 2002016656 A2 20020228 (200233)* EN 40p C12Q001-68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001085467 A 20020304 (200247) C12Q001-68
ADT WO 2002016656 A2 WO 2001-US41814 20010820; AU 2001085467 A AU 2001-85467 20010820
FDT AU 2001085467 A Based on WO 200216656
PRAI US 2000-226759P 20000821
IC ICM C12Q001-68
AB WO 200216656 A UPAB: 20020524
NOVELTY - Detecting (I) one or more mutation(s) in a human ortholog of the murine scurfy gene, termed **FOXP3** gene specific nucleic acid, comprising isolating a population of nucleic acids from a biological sample, amplifying a **FOXP3** specific nucleic acid sequence from the isolated population of nucleic acids, and detecting the mutation in the **FOXP3** gene, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) detecting (II) the presence of a mutated scurfy/**FOXP3** nucleic acid sequence in a biological sample from a subject, by contacting a **FOXP3** specific nucleic acid probe under hybridizing conditions with either:

(a) test nucleic acid molecules isolated from the biological sample; or

(b) nucleic acid molecules synthesized from RNA molecules (the probe recognizes at least a portion of nucleotide sequence of the **FOXP3** nucleic acid); and

(c) detecting the formation of hybrids of the nucleic acid probe and (a) or (b);

(2) an isolated nucleic acid comprising an oligonucleotide capable of specifically binding to a polynucleotide encoding a mutation within the forkhead/winged helix-like domain of the **FOXP3** protein; and

(3) a kit for detection of a mutated **FOXP3** gene or its

polynucleotide expression product, comprising at least one oligonucleotide capable of hybridizing specifically to a mutated region of the gene or its polynucleotide expression product, a carrier, reagent(s), an optional control sample, and instructions for carrying out the assay.

USE - (I) is useful for detecting mutations of the **FOXP3** gene, and (II) is useful for diagnosis **FOXP3** gene-related diseases in humans. Mutations in the human scurfy/**FOXP3** gene causing human X-linked disorders which may or may not be similar to scurfy disease in mice, may be detected. An e.g. of such a human disorder is immune dysregulation, polyendocrinopathy, enteropathy, or X-linked syndrome.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-E01; B04-E05; B04-L04A; B04-L04B; B11-A02; B11-C08E3; B11-C08E4; B11-C08E5; B11-C08F1; B11-C08F2; B11-C10; B12-K04A3; B12-K04E; B12-K04F; D05-A02B; D05-H09; D05-H12; D05-H12D1; D05-H18; D05-H18A; D05-H18B; D05-J

TECH UPTX: 20020524

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The human **FOXP3** gene specific nucleic acid is genomic DNA, mRNA or cDNA and is amplified by a polymerase chain reaction (PCR) utilizing a pair of oligonucleotides specific for human **FOXP3** genomic DNA. Detecting mutation in the **FOXP3** gene further comprises, sequencing the amplified **FOXP3** specific nucleic acid sequence, and comparing the sequence of the amplified **FOXP3** sequence with the sequence of wild-type **FOXP3** of 1869 or 20000 bp given in the specification, where a difference between the sequence of the amplified **FOXP3** and wild-type **FOXP3** indicates the presence of a **FOXP3** mutation.

In (II), the test nucleic acid molecule is obtained by reverse transcription-PCR (RT-PCR), performed using at least two oligonucleotide primers, or is a genomic DNA.

ABEX

WIDER DISCLOSURE - Also disclosed are the following:
(1) polypeptide encoded by a human FOXP3 gene or its oligonucleotide fragment;
(2) antibodies capable of binding to the above polypeptide and use of the antibodies for detecting the mutated protein;
(3) pharmaceutical compositions comprising the above antibodies or proteins that modulate the immune system;
(4) oligonucleotide fragments (including probes and primers) which are based upon the sequence of the human FOXP3 gene;
(5) a kit for detection of a mutated FOXP3 gene or its expression product, comprising (2); and
(6) selecting and/or isolating molecules that are capable of modulating the immune system.

SPECIFIC OLIGONUCLEOTIDES - In (I), the pair of oligonucleotides for amplifying genomic DNA is chosen from:
(i) GGTTGGCCCTGTGATTTAT and CCCCCGCCGTGCCTACCT;
(ii) GCCAATGCCTGCTTTGACCAG and CCAGTGCCACAGTAAAGGTCG;
(iii) CCATGTGGGCTTGCAGTGCAG and GCTCACAGCCAAGGATCTGGG;
(iv) TGGGAGTCAGGGTTTTCGAGG and TTATTGGGATGAAGCCTGAGC;
(v) CAGAGCATTGAGCCAGACCAG and CCAGCAGTCTGAGTCTGCCAC;
(vi) GTGGGAAGTTTAAGCCTCTGG and TTGTGAGCGGATGCATTTTC;
(vii) TGTCAGGTGCTCAGCAAACAG and CATGAGGGGTCACATTTGAGG;
(viii) ACCCCAAGTTTGGGGAATGTG and CAGTTTGGCCCCTGTTCGTCC; and
(ix) ACGGGATGTGGGTTGTTGGT and GGGTTGTCAGGGCTGTGCTTGTGT.
The pair of oligonucleotides for amplifying mRNA or cDNA is CTTTTCTGTCAGTCCACTTCAC and GGCAAGACAGTGGAAACCTCAC (claimed).

EXAMPLE - Genomic DNA was extracted from peripheral blood or from cultured

skin fibroblasts. Nine human FOXP3 gene amplicons representing coding exons 1-11, the 3' UTR, one 5' non-coding exon, as well as at least 50 bases of flanking intronic sequence for each exon were amplified by polymerase chain reaction (PCR) from the genomic DNAs of subjects and unaffected controls.
Primers used for 5' non-coding exon were: GGTTGGCCCTGTGATTTAT and CCCCCGCCGTGCCTACCT, the primers used for exon 1 were GCCAATGCCTGCTTTGACCAG and CCAGTGCCACAGTAAAGGTCG, the primers used for exons 2 and 3 were: CCATGTGGGCTTGCAGTGCAG and GCTCACAGCCAAGGATCTGGG. Exons 4+5, 6+7, 8, 9, 10+11, and 3' UTR were also amplified using specific primers given in the specification.
Amplicon products were purified and subjected to direct sequencing. Sequence data were analyzed using Sequencer program. Full sequence from both strands of all amplicons was obtained for the mutation analysis.
In addition to the patients and unaffected family members analyzed for this study, FOXP3 gene exons were sequenced from a number of unrelated normal control genomic DNAs. Sequence of all nine amplicons was obtained from a set of 90 ethnically diverse individuals from the NIGMS Human Variation Collection, panels HD01-HD09. Exons 10 and 11, encoding the forkhead domain, were also sequenced in an additional 150 individuals from the NIGMS DNA Polymorphism Discovery Resource.
The FOXP3 mutations were 1189C to T, Del1290 to 1309/insTGG, 1150G to A in exon 11, and 1113G to T in exon 10.

L84 ANSWER 2 OF 2 WPIX (C) 2002 THOMSON DERWENT
AN 2000-224336 [19] WPIX
DNN N2000-168095 DNC C2000-068505
TI Novel nucleic acid molecule encoding **Fkhsf** useful for identifying and treating lymphoproliferative disorders, especially scurfy related disorders.
DC B04 D16 S03
IN BRUNKOW, M E; HJERRILD, K A; JEFFERY, E W; RAMSDELL, F
PA (DARW-N) DARWIN DISCOVERY LTD
CYC 89
PI WO 2000009693 A2 20000224 (200019)* EN 59p C12N015-12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9955594 A 20000306 (200030) C12N015-12
EP 1105479 A2 20010613 (200134) EN C12N015-12
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6414129 B1 20020702 (200248) C07H021-02
ADT WO 2000009693 A2 WO 1999-US18407 19990811; AU 9955594 A AU 1999-55594 19990811; EP 1105479 A2 EP 1999-942154 19990811, WO 1999-US18407 19990811; US 6414129 B1 Provisional US 1998-96195P 19980811, US 1999-372668 19990811
FDT AU 9955594 A Based on WO 200009693; EP 1105479 A2 Based on WO 200009693
PRAI US 1998-96195P 19980811; US 1999-372668 19990811
IC ICM C07H021-02; C12N015-12
ICS A61K038-17; C07H021-04; C07K014-47; C07K016-18; C12N005-00; C12N015-63; C12P021-06; C12Q001-68; G01N033-50
AB WO 200009693 A UPAB: 20000419
NOVELTY - An **Fkhsf** protein (I) comprising a sequence of 429 amino acids, given in the specification, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a nucleic acid (II) encoding (I);
(2) a vector (III) comprising (II);
(3) a recombinant host cell (IV) comprising (III);
(4) preparation of (I);

(5) an antibody (Ab) or its fragment capable of specifically binding to (II);

(6) a fusion protein comprising (I);

(7) detecting (d1) the presence of (II) in biological sample of the subject by detecting the hybrid formed by contacting **Fkhsf** specific nucleic acid probe to the test nucleic acid isolated from the biological sample or to the nucleic acids synthesized from RNA molecules;

(8) detecting (d2) the presence of (I) in biological sample by contacting (Ab) with biological sample and detecting the bound antibody complex;

(9) an isolated oligonucleotide (Ia) capable of hybridizing (II);

(10) introduction of (II) into an animal; and

(11) a transgenic non-human animal capable of expressing a transgene containing (II).

USE - The detection of (I) or (II) in the biological sample of the subject is used to diagnose lymphoproliferative disorders, particularly scurfy related disorders. These disorders may be treated by administering (I) or (II).

ADVANTAGE - Identification of (I) has led to the development of assays which may be utilized to select molecules that can act as agonists or antagonists of the immune system.

Dwg.0/10

FS CPI EPI

FA AB; DCN

MC CPI: B04-C01G; B04-E02F; B04-E05; B04-E08; B04-G01; B04-N02A0E; B04-P01A0E; B11-A; B11-C08E5; B12-K04F; B14-F02E; D05-H08; D05-H09; D05-H11; D05-H12A; D05-H12C; D05-H12D1; D05-H12E; D05-H14; D05-H16A; D05-H17A6; D05-H17C; D05-H18

EPI: S03-E14H

TECH UPTX: 20000419

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (IV) is cultured and (II) is isolated (claimed). (I) can be obtained by PCR mutagenesis, chemical mutagenesis, by forced nucleotide misincorporation or by use of randomly mutagenized oligonucleotides. Preferred Nucleic Acid: (I) may be a nucleic acid molecule encoding a polypeptide of sequence comprising 429 or 431 amino acids, a nucleic acid molecule that hybridizes to a sequence of 2160 or 1869 nucleotides, its complement or a nucleic acid molecule encoding the functional fragment of (II). (I) is not JM2. Preferred Vector: (III) is a viral vector which may be a retrovirus, adenovirus, herpesvirus, adeno-associated virus or alphavirus and is operably linked to a promoter. Preferred Antibody: (Ab) is a polyclonal, humanized or a monoclonal antibody of murine or human origin and may comprise fragment F(ab')2, F(ab)2, Fab', Fab, Fv, sFv or minimal recognition unit. Preferred Method: Test nucleic acid for (d1) is obtained by reverse transcriptase-PCR. (Ab) used in (d2) comprises a detectable label which may be a radioisotope, a fluorescent label, chemiluminescent label, enzyme label, bioluminescent label or colloidal gold. Introduction of (I) is by viral or plasmid vector and is administered in vivo. Ex vivo administration of (I) to cells, preferably hematopoietic T-cells and then administering the cells to the animals, preferably humans, monkeys, dogs, cats, rats and mice is also preferable.

ABEX

WIDER DISCLOSURE - The following are disclosed: (1) selecting and/or isolating candidate molecules capable of modulating immune system; (2) determining whether the selected molecule is capable of modulating the immune system; and (3) pharmaceutical compositions for diagnosing scurfy related diseases comprising candidate molecules.

SPECIFIC SEQUENCES - (I) comprises a sequence of 2160 nucleotides which encodes a sequence of 429 amino acids (claimed).

EXAMPLE - 5 mug of total RNA obtained from mouse spleen was extended and first strand cDNA was generated by oligo dT priming using reverse

transcriptase. An aliquot of the first strand cDNA was amplified by PCR using primers 5-GCAGATCTCCTGACTCTGCCTTC-3 and 5-GCAGATCTGACAAGCTGTGTCTG-3 and one unit of Taq polymerase. cDNA encoding the complete mouse Fkhsf protein was obtained.

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 07:27:58 ON 16 AUG 2002
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FILE COVERS 1907 - 16 Aug 2002 VOL 137 ISS 7
FILE LAST UPDATED: 14 Aug 2002 (20020814/ED)

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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all tot

L94 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:158041** HCAPLUS
DN **136:195293**
TI Methods for detecting mutations in the human **scurfy**/**FOXP3** gene
IN **Brunkow, Mary E.**
PA Celltech R & D, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 13
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002016656	A2	20020228	WO 2001-US41814	20010820

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001085467 A5 20020304 AU 2001-85467 20010820
PRAI US 2000-226759P P 20000821
WO 2001-US41814 W 20010820
AB Methods and compns. are provided for detecting a mutation of the human ortholog of the murine **scurfy** gene, called **FOXP3**. Also provided are oligonucleotide primers for amplifying specific regions of the **FOXP3** gene. Such primers find use in providing polynucleotides from humans suspected of having a **FOXP3** gene mutation because of family history and/or clin. indications. The method is exemplified by the identification of five different mutations in **FOXP3** gene from **IPEX** families using primers targeted to different exons or the non-coding regions.
ST human **FOXP3** gene mutation detection RT PCR primer
IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**FOXP3** allele specific; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Gene, animal
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**FOXP3**; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT PCR (polymerase chain reaction)
(RT-PCR (reverse transcription-PCR), assay for gene **FOXP3** mutations; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT PCR (polymerase chain reaction)
(assay for gene **FOXP3** mutations; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Mutation
(deletion, in human gene **FOXP3**; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Test kits
(diagnostic; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Protein motifs
(forkhead/winged helix-like domain, of **FOXP3** gene protein, primers specific for the coding region for; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT DNA
RL: ANT (Analyte); ANST (Analytical study)
(genomic, of human gene **FOXP3**; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Mutation
(in human gene **FOXP3**; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT DNA sequences
Human
Nucleic acid hybridization
(methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Diagnosis
(mol.; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Genetic polymorphism
(of human gene **FOXP3**; methods for detecting mutations in

human **scurfy/FOXP3** gene)
IT cDNA
mRNA
RL: ANT (Analyte); ANST (Analytical study)
(of human gene **FOXP3**; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT Mutation
(substitution, in human gene **FOXP3**; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT 401554-27-6 401554-28-7 401554-29-8 401554-30-1 401554-31-2
401554-32-3 401554-33-4 401554-34-5 401554-35-6 401554-36-7
401554-37-8 401554-38-9 401554-39-0 401554-40-3 401554-41-4
401554-42-5 401554-43-6 401554-44-7 401554-45-8 401554-46-9
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence of primer; methods for detecting mutations in human **scurfy/FOXP3** gene)
IT 401554-25-4, DNA (human gene **FOXP3** cDNA plus flanks)
401554-26-5, DNA (human gene **FOXP3** plus flanks)
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; methods for detecting mutations in human **scurfy/FOXP3** gene)

L94 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:884108** HCAPLUS
DN **136:133586**
TI The amount of **scurfin** protein determines peripheral T cell number and responsiveness
AU Khattri, Roli; Kasprowicz, Deborah; Cox, Tom; Mortrud, Marty; Appleby, Mark W.; **Brunkow, Mary E.**; Ziegler, Steven F.; **Ramsdell, Fred**
CS Celltech R and D, Inc., Bothell, WA, 98021, USA
SO Journal of Immunology (2001), 167(11), 6312-6320
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB In the absence of the recently identified putative transcription factor **scurfin**, mice develop a lymphoproliferative disorder resulting in death by 3 wk of age from a pathol. that resembles TGF-.beta. or CTLA-4 knockout mice. In this report, we characterize mice that overexpress the **scurfin** protein and demonstrate that these animals have a dramatically depressed immune system. Mice transgenic for the **Foxp3** gene (which encodes the **scurfin** protein) have fewer T cells than their littermate controls, and those T cells that remain have poor proliferative and cytolytic responses and make little IL-2 after stimulation through the TCR. Although thymic development appears normal in these mice, peripheral lymphoid organs, particularly lymph nodes, are relatively acellular. In a sep. transgenic line, forced expression of the gene specifically in the thymus can alter thymic development; however, this does not appear to affect peripheral T cells and is unable to prevent disease in mice lacking a functional **Foxp3** gene, indicating that the **scurfin** protein acts on peripheral T cells. These data indicate a crit. role for the **Foxp3** gene product in the function of the immune system, with both the no. and functionality of peripheral T cells under the aegis of the **scurfin** protein.
ST **scurfin** immunity T lymphocyte
IT CD4-positive T cell
CD8-positive T cell
Immunity

Lymph node
Thymus gland
(amt. of **scurfin** protein dets. peripheral T cell no. and responsiveness)

IT Interleukin 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(amt. of **scurfin** protein dets. peripheral T cell no. and responsiveness)

IT T cell (lymphocyte)
(cytotoxic; amt. of **scurfin** protein dets. peripheral T cell no. and responsiveness)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene **Foxp3**; amt. of **scurfin** protein dets. peripheral T cell no. and responsiveness)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**scurfin**; amt. of **scurfin** protein dets. peripheral T cell no. and responsiveness)

L94 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:850281** HCAPLUS
DN **136:323889**
TI A rare polyadenylation signal mutation of the **FOXP3** gene (AAUAAA.fwdarw.AAUGAA) leads to the **IPEX** syndrome
AU Bennett, Craig L.; **Brunkow, Mary E.**; **Ramsdell, Fred**; O'Briant, Kathy C.; Zhu, Qili; Fuleihan, Ramsay L.; Shigeoka, Ann O.; Ochs, Hans D.; Chance, Phillip F.
CS Division of Genetics and Development, Department of Pediatrics, University of Washington School of Medicine, Seattle, WA, 98195, USA
SO Immunogenetics (2001), 53(6), 435-439
CODEN: IMNGBK; ISSN: 0093-7711
PB Springer-Verlag
DT Journal
LA English
CC 15-8 (Immunochemistry)
Section cross-reference(s): 14
AB The mouse **scurfy** gene, **Foxp3**, and its human orthologue, **FOXP3**, which maps to Xp11.23-Xq13.3, were recently identified by positional cloning. Point mutations and microdeletions of the **FOXP3** gene were found in the affected members of eight of nine families with **IPEX** (immune dysfunction, polyendocrinopathy, enteropathy, X-linked; OMIM 304930). We evaluated a pedigree with clin. typical **IPEX** in which mutations of the coding exons of **FOXP3** were not detected. Our reevaluation of this pedigree identified an A.fwdarw.G transition within the first polyadenylation signal (AAUAAA.fwdarw.AAUGAA) after the stop codon. The next polyadenylation signal is not encountered for a further 5.1 kb. This transition was not detected in over 212 normal individuals (.apprx.318 X chromosomes), excluding the possibility of a rare polymorphism. We suggest that this mutation is causal of **IPEX** in this family by a mechanism of nonspecific degrdn. of the **FOXP3** gene message.
ST **FOXP3** gene mutation polyadenylation signal **IPEX** syndrome
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**FOXP3**; rare polyadenylation signal mutation of the **FOXP3** gene leads to the **IPEX** syndrome)
IT Immunity
(disorder, immune dysfunction, polyendocrinopathy, enteropathy (**IPEX** syndrome); rare polyadenylation signal mutation of the **FOXP3** gene leads to the **IPEX** syndrome)
IT Genetic element

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (polyadenylation signal; rare polyadenylation signal mutation of the **FOXP3** gene leads to the **IPEX** syndrome)

IT Human
Mutation
(rare polyadenylation signal mutation of the **FOXP3** gene leads to the **IPEX** syndrome)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(23) Wildin, R; Nat Genet 2001, V27, P18 HCAPLUS

L94 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:763740 HCAPLUS

DN 136:52577

TI **Scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation

AU Schubert, Lisa A.; **Jeffery, Eric**; Zhang, Yi; **Ramsdell, Fred**; Ziegler, Steven F.

CS Immunology Program, Virginia Mason Research Center, Seattle, WA, 98101, USA

SO Journal of Biological Chemistry (2001), 276(40), 37672-37679
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 15-7 (Immunochemistry)
Section cross-reference(s): 3

AB We have recently identified and cloned **Foxp3**, the gene defective in mice with the **scurfy** mutation. The immune dysregulation documented in these mice and in humans with mutations in the orthologous gene indicates that the **foxp3** gene product, **scurfin**, is involved in the regulation of T cell activation and differentiation. The autoimmune state obsd. in these patients with the immune dysregulation polyendocrinopathy, enteropathy, X-linked syndrome, or X-linked autoimmunity-allergic dysregulation syndrome also points to a crit. role for **scurfin** in the regulation of T cell homeostasis. **FOXP3** encodes a novel member of the forkhead family of transcription factors. Here we demonstrate that this structural domain is required for nuclear localization and DNA binding. **Scurfin**, transiently expressed in heterologous cells, represses transcription of a reporter contg. a multimeric forkhead binding site. Upon overexpression

in CD4 T cells, **scurfin** attenuates activation-induced cytokine prodn. and proliferation. We have identified FKH binding sequences adjacent to crit. NFAT regulatory sites in the promoters of several cytokine genes whose expression is sensitive to changes in SFN abundance. Our findings indicate that the ability of **scurfin** to bind DNA, and presumably repress transcription, plays a paramount role in detg. the amplitude of the response of CD4 T cells to activation.

ST **scurfin** binding DNA transcription repression

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**Foxp3; scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation)

IT T cell (lymphocyte)
(activation; **scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation)

IT Immunity
(autoimmunity, X-linked; **scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation in)

IT Transcriptional regulation
(repression; **scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation by binding to)

IT CD4-positive T cell
Intestine, disease
(**scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation in)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**scurfin; scurfin** (**FOXP3**) acts as a repressor of transcription and regulates T cell activation)

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L94 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:26869** HCAPLUS
DN **134:220984**
TI The immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (**IPEX**) is caused by mutations of **FOXP3**
AU Bennett, Craig L.; Christie, Jacinda; **Ramsdell, Fred**; **Brunkow, Mary E.**; Ferguson, Polly J.; Whitesell, Luke; Kelly, Thaddeus E.; Saulsbury, Frank T.; Chance, Phillip F.; Ochs, Hans D.
CS Division of Genetics and Development, University of Washington, Seattle, WA, USA
SO Nature Genetics (2001), 27(1), 20-21
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America Inc.
DT Journal
LA English
CC 14-14 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 15
AB **IPEX** is a fatal disorder characterized by immune dysregulation, polyendocrinopathy, enteropathy and X-linked inheritance (MIM 304930). We present genetic evidence that different mutations of the human gene **FOXP3**, the ortholog of the gene mutated in **scurfy** mice (**Foxp3**), causes **IPEX** syndrome. Recent linkage anal. studies mapped the gene mutated in **IPEX** to an interval of 17-20-cM at Xp11.23-Xq13.3.
ST **IPEX** syndrome **FOXP3** mutation
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(**FOXP3**; immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (**IPEX**) is caused by mutations of **FOXP3**, in humans)
IT Disease, animal
(genetic; immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (**IPEX**) is caused by mutations of **FOXP3**, in humans)
IT Genetic inheritance
Mutation
(immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (**IPEX**) is caused by mutations of **FOXP3**, in humans)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

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L94 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:26868** HCAPLUS
DN **134:220830**
TI X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is the human equivalent of mouse **scurfy**
AU Wildin, Robert S.; **Ramsdell, Fred**; Peake, Jane; Faravelli, Francesca; Casanova, Jean-Laurent; Buist, Neil; Levy-Lahad, Ephrat; Mazzella, Massimo; Goulet, Olivier; Perroni, Lucia; Bricarelli, Franca Dagna; Byrne, Geoffrey; McEuen, Mark; Proll, Sean; Appleby, Mark; **Brunkow, Mary E.**
CS Department of Molecular and Medical Genetics, Oregon Health Sciences University, Portland, OR, L103A, USA
SO Nature Genetics (2001), 27(1), 18-20
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America Inc.
DT Journal
LA English
CC 14-8 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB To det. whether human X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome (**IPEX**; MIM 304930) is the genetic equiv. of the **scurfy** (**sf**) mouse, the authors sequenced the human ortholog (**FOXP3**) of the gene mutated in **scurfy** mice (**Foxp3**), in **IPEX** patients. The authors found four non-polymorphic mutations. Each mutation affects the forkhead/winged-helix domain of the **scurfin** protein, indicating that the mutations may disrupt crit. DNA interactions.
ST X linked neonatal diabetes enteropathy endocrinopathy syndrome **FOXP3** mutation; **scurfy** mouse X linked neonatal diabetes enteropathy endocrinopathy syndrome
IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**FOXP3**; X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)
IT Diabetes mellitus
Intestine, disease
Mouse
Newborn
(X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)
IT Mutation
(deletion; X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)
IT Endocrine system
(disease; X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)
IT Protein motifs
(forkhead/winged-helix domain; X-linked neonatal diabetes mellitus,

enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)

IT Mutation
(insertion; X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)

IT Mutation
(missense; X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**scurfin**; X-linked neonatal diabetes mellitus, enteropathy and endocrinopathy syndrome is human equiv. of mouse **scurfy** in relation to mutation in **scurfin** gene)

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L94 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS

AN **1999:137499** HCAPLUS

DN **130:310562**

TI Cellular and molecular characterization of the **scurfy** mouse mutant

AU Clark, Lisa B.; Appleby, Mark W.; **Brunkow, Mary E.**; Wilkinson, J. Erby; Ziegler, Steven F.; **Ramsdell, Fred**

CS Chiroscience R&D, Inc., Seattle, WA, 98021, USA

SO Journal of Immunology (1999), 162(5), 2546-2554
CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

CC 15-8 (Immunochemistry)

AB Mice hemizygous (Xsf/Y) for the X-linked mutation **scurfy** (**sf**) develop a severe and rapidly fatal lymphoproliferative disease mediated by CD4+CD8- T lymphocytes. We have undertaken phenotypic and functional studies to more accurately identify the immunol. pathway(s) affected by this important mutation. Flow cytometric analyses of lymphoid cell populations reveal that **scurfy** syndrome is characterized by changes in several phenotypic parameters, including an increase in Mac-1+ cells and a decrease in B220+ cells, changes that may result from the prodn. of extremely high levels of the cytokine granulocyte-macrophage CSF by **scurfy** T cells. **Scurfy** T cells also exhibit strong up-regulation of cell surface Ags indicative of in vivo activation, including CD69, CD25, CD80, and CD86. Both **scurfy** and normal T cells are responsive to two distinct signals provided by the TCR and by ligation of CD28; **scurfy** cells, however, are hyperresponsive to TCR ligation and exhibit a decreased requirement for costimulation through CD28 relative to normal controls. This hypersensitivity may result, in

part, from increased costimulation through B7-1 and B7-2, whose expression is up-regulated on **scurfy** T cells. Although the specific defect leading to this hyperactivation has not been identified, we also demonstrate that **scurfy** T cells are less sensitive than normal controls to inhibitors of tyrosine kinases such as genistein and herbimycin A, and the immunosuppressant cyclosporin A. One interpretation of our data would suggest that the **scurfy** mutation results in a defect, which interferes with the normal down-regulation of T cell activation.

ST **scurfy** mouse T lymphocyte activation GM CSF

IT Cell activation
(T cell; cellular and mol. characterization of the **scurfy** mouse mutant)

IT T cell (lymphocyte)
(activation; cellular and mol. characterization of the **scurfy** mouse mutant)

IT CD4-positive T cell
Lymphoproliferative disorders
Mouse
Signal transduction, biological
(cellular and mol. characterization of the **scurfy** mouse mutant)

IT CD80 (antigen)
CD86 (antigen)
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(cellular and mol. characterization of the **scurfy** mouse mutant)

IT CD69 (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(cellular and mol. characterization of the **scurfy** mouse mutant)

IT CD28 (antigen)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cellular and mol. characterization of the **scurfy** mouse mutant)

IT TCR (T cell receptors)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cellular and mol. characterization of the **scurfy** mouse mutant)

IT Chromosome
(mouse X; cellular and mol. characterization of the **scurfy** mouse mutant)

IT Mutation
(**scurfy**; cellular and mol. characterization of the **scurfy** mouse mutant)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**scurfy**; cellular and mol. characterization of the **scurfy** mouse mutant)

IT Interleukin 2 receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.alpha.-chain; cellular and mol. characterization of the **scurfy** mouse mutant)

IT 83869-56-1, Gm-csf
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(cellular and mol. characterization of the **scurfy** mouse mutant)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
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=> d his

(FILE 'HOME' ENTERED AT 06:30:37 ON 16 AUG 2002)
SET COST OFF

FILE 'MEDLINE' ENTERED AT 06:30:53 ON 16 AUG 2002
E BRUNKOW M/AU
L1 14 S E3-E5
E JEFFERY E/AU
L2 15 S E3,E6
E HJERRILD K/AU
L3 8 S E3,E4
E RAMSDELL F/AU
L4 42 S E3-E5
E DARWIN/CS
L5 556 S E3-E17
L6 69 S L1-L4
E SCURFY
L7 25 S E3
E SCURF
L8 32 S E3-E5
L9 7 S L8 AND L7
L10 9 S FOXP3

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L11           0 S FOX P3
L12          50 S L7-L10
                E SKH
                E FKH
L13           0 S FKH SF
L14           0 S FKHSF
L15           0 S ?FKHSF?
L16          50 S (SCURF? OR FOXP3?)/TI,BI
L17          50 S L12,L16
                E CD4-POSITIVE T-LYMPHOCYTES/CT
                E E3+ALL
L18           5 S E21+NT AND L17
L19          10 S E20+NT AND L17
L20          10 S L18,L19
L21          24 S (D12. OR D13.)/CT AND L17
L22          25 S (G1. OR G3. OR G5.)/CT AND L17
L23          33 S (E1. OR E5.)/CT AND L17
L24          24 S A11./CT AND L17
L25          10 S D24./CT AND L17
L26          37 S L18-L25
                SEL DN AN 3 8 10 18 20 22 32 33 35 36 37
L27          11 S L26 AND E1-E33
L28          26 S L26 NOT L27
L29          13 S L17 NOT L26
                SEL DN AN 1
L30           1 S L29 AND E34-E36
L31          27 S L28,L30
                E SF/GEN
L32           7 S E3
L33           8 S E4-E9
L34           3 S L31 AND L32,L33
L35          12 S L32,L33 NOT L34
L36          27 S L31,L34
L37           7 S L6 AND L17
L38           0 S L6 AND L32,L33
L39          27 S L36,L37
L40          11 S L39 AND PY<=1998
L41          16 S L39 AND SF
L42           9 S L40 AND L41
L43          11 S L40,L42
L44          16 S L39,L41 NOT L43

     FILE 'MEDLINE' ENTERED AT 07:01:42 ON 16 AUG 2002

     FILE 'BIOSIS' ENTERED AT 07:02:22 ON 16 AUG 2002
                E SCURF
L45          51 S E4-E10
                E FKH
L46           1 S E45
L47           0 S FKH (L) SF
L48           1 S FKH (L) L45
L49           9 S FOXP3
L50          52 S L45,L48,L49
                E SF
L51          18 S SF AND L50
L52          52 S L50,L51
L53           5 S L52 AND IPEX
L54          52 S L52,L53
L55          31 S L54 AND PY<=1998
                SEL DN AN 2 3 10 13 22-31
L56          17 S L55 NOT E1-E28
                E BRUNKOW M/AU
L57           6 S E3-E6 AND L54
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                E JEFFERY E/AU
L58           3 S E3,E9,E10 AND L54
                E HJERRILD K/AU
L59           2 S E3,E4,E6-E8 AND L54
                E RAMSDELL F/AU
L60           7 S E3-E6 AND L54
L61          24 S L57-L60,L46,L56

     FILE 'BIOSIS' ENTERED AT 07:12:17 ON 16 AUG 2002

     FILE 'HCAPLUS' ENTERED AT 07:12:31 ON 16 AUG 2002
                E FKH
L62           2 S E117
                E SCURF
L63         271 S E3-E12
L64       10660 S SF
L65           8 S FOXP3
L66           5 S IPEX
L67          21 S 3/SC,SX AND L63
L68         788 S 3/SC,SX AND L64
L69          24 S L62,L65,L66,L67
L70           7 S L68 AND L69
L71          24 S L69,L70
L72           9 S L71 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
                SEL DN AN 2 5
L73           7 S L72 NOT E1-E6
L74           8 S L62,L73
L75           8 S L74 AND L62-L74

     FILE 'REGISTRY' ENTERED AT 07:18:25 ON 16 AUG 2002
                E FKH
L76           4 S E77

     FILE 'HCAPLUS' ENTERED AT 07:18:49 ON 16 AUG 2002
L77           2 S L76
L78           8 S L77,L75

     FILE 'HCAPLUS' ENTERED AT 07:19:06 ON 16 AUG 2002

     FILE 'REGISTRY' ENTERED AT 07:19:22 ON 16 AUG 2002

     FILE 'WPIX' ENTERED AT 07:20:07 ON 16 AUG 2002
                E FKHSF
L79           1 S E3
L80           0 S FKH (L) SF
L81           1 S FOXP3
L82           1 S IPEX
L83           3 S L79,L81,L82
L84           2 S L83 NOT D13/DC

     FILE 'WPIX' ENTERED AT 07:21:36 ON 16 AUG 2002

     FILE 'HCAPLUS' ENTERED AT 07:22:10 ON 16 AUG 2002
                E BURNKOW M/AU
                E BRUNKOW M/AU
L85          20 S E4-E7
                E JEFFERY E/AU
L86           9 S E3,E10,E11
                E HJERRILD K/AU
L87          11 S E5-E7
                E RAMSDELL F/AU
L88          35 S E4-E6
L89          62 S L85-L88
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L90          60 S L89 NOT L78
L91           7 S L90 AND L62-L66
L92           2 S L90 AND SF
                SEL DN AN L90 3 5 6 9 10 13
L93           6 S L90 AND E1-E18
L94           7 S L91-L93

     FILE 'HCAPLUS' ENTERED AT 07:27:58 ON 16 AUG 2002
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